THE F-WAVE AND ITS USE IN THE ELECTRODIAGNOSIS OF NEUROLOGICAL DISORDERS

by

William N. Macleod

MBChB, MRCP.

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Dedicated to

ROBERT, ANGELA
and SARAH

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ABBREVIATIONS/UNITS OF MEASUREMENT

Ca	:	circa
CT Scan	:	computerised tomographic scan
EMG	:	electromyography
MRI	:	magnetic resonance image
mm	:	millimeter
ms	:	millisecond
mV	:	millivolt
m/s	:	metres per second
µV	:	microvolt
µs	:	microsecond
S.D.	:	standard deviation
SFEMG	:	single fibre electromyography

GLOSSARY OF TERMS

Central motor conduction latency

The time taken for transmission of the fastest conducted motor impulse from a stimulus site on motor axons (usually over a mixed peripheral nerve) to the spinal cord.

F-wave - F-response - F-discharge

These 3 terms have been used synonymously. See text for the nature of the F-wave.

F-wave persistence value

A measure of the frequency of recurrent motor discharges from either a test motor neurone pool (see Chapters 2, 4, 5 and 6) or a part of it, e.g. a single motor neurone (see Chapter 1.4.2). In the experiments of this thesis, the frequency at which surface recorded F-waves >40 μV (peak to peak amplitude) appear when a train of 100 supramaximal stimuli is delivered to the test muscle's mixed nerve has been termed the F-wave persistence value, i.e. number of F-waves, > 40 μV, per 100 M waves.

F chronodispersion

The latency range of a series of consecutive F-waves, measured from the initial deflection of the earliest and latest recorded F-waves.

F-ratio

A ratio which represents a comparison of impulse transmission latencies across the proximal and distal segments of motor axons transmitting the earliest surface recorded F-response. For calculation of, and uses for, the F-ratio see 2.1.4.

F-wave conduction velocity

An estimate of motor conduction velocity in the proximal segment of motor fibres transmitting the fastest conducted F-response to a test muscle. For formula to compute the F-wave conduction velocity, see 2.1.5.

Jitter

Variations in the onset of depolarisation in a muscle fibre when a series of action potentials are recorded using the single fibre EMG electrode. Jitter can be measured for an orthodromically conducted motor response, M wave jitter, or for an antidromically activated recurrent motor response, F-wave jitter.

"Late" responses

In this thesis the term describes muscle action potentials activated by electrical stimuli, to either a mixed nerve or a muscle, whose latencies are greater than that of the M wave: the term embraces delayed M components, F-waves, axon reflexes and reflexly activated muscle responses.

M wave - M response

These 2 terms are used interchangeably. The compound muscle action potential recorded from a muscle, a single motor unit, part of a single motor unit or a number of motor units resulting from orthodromic propagation of a motor nerve impulse.

%Repeater F-wave value

The Repeater F-wave count ÷ the F-wave persistence value, expressed as a percentage.

"Turnaround" time

This is a vague descriptive term which appears in the literature on the F-response. It refers to the time a backfired motor neurone takes to issue a recurrent motor discharge.

Repeater F-wave

An individual F-wave (>40 μV, peak-peak) recorded from a muscle more than once i.e. an F-wave, characterised by latency and configuration, which is generated twice or more by a test motor neurone pool when a train of supramaximal stimuli is delivered to the motor axons under test.

Repeater F-wave count

The total number of F-wave sweeps in which a Repeater F-wave is recorded. (The value is derived from 100 F-wave sweeps in the experiments of this thesis).

DECLARATION OF ORIGINALITY

All the original work recorded in this thesis was conducted by the author or done under his direct supervision in the Clinical Neurophysiology Laboratory, Department of Medical Neurology, Dundee Royal Infirmary, Dundee, Scotland, or in the Clinical Neurophysiology Laboratory, Massachusetts General Hospital, Boston, Massachusetts, U.S.A., between 1984 and 1988. This thesis has not been submitted elsewhere for any degree and was written by me, alone.

William N Macleod.

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The experiments required large numbers of volunteers and I found that many patients, friends and colleagues were refreshingly helpful and I am grateful to them all.

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The work detailed in this thesis was started when the late Dr J.A.R. Lenman was still alive. His encouragement was vital and led to a year being spent in the Clinical Neurophysiology Laboratory of the Massachusetts General Hospital in Boston. That Laboratory was run by Professor Robert R. Young and in that Department some of the early and important research into the clinical applications of the F-wave was done. I found, there, a stimulating atmosphere and gained greatly from discussions with Professor Young and his colleague, Dr B.T. Shahani, with whom I collaborated on some

work on the F-wave.

Ms Morag Wilson has produced high quality illustrations of the F-response sweeps and Miss Maureen Sneddon kindly made up histograms and diagrams.

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ABSTRACT

This is a study of an electrophysiological artefact, the F-wave. Until now, the latency of the F-wave has been the only F-wave parameter used in clinical electrodiagnosis.

Personal observations and theoretical considerations suggested that disorders of the lower motor neurone could modify F-wave discharge patterns. Quantification of any such effect might provide a new method of identifying peripheral nervous system lesions. This concept forms the basis for the majority of experiments described. The other concept concerns a new method of evoking F-waves. As some muscles' nerves are inaccessible to percutaneous electrical stimulation the feasibility and utility of a new technique for eliciting F-responses, by stimulating the test muscle over its motor point, were considered.

Initial experiments tested the first hypothesis and the practicability of recording F-waves evoked from the motor point. Subsequent experiments were designed with the aim of developing the above concepts into methods for detecting and localising peripheral nerve lesions.

The F-wave generating activity of different motor neurone pools in health and the influence of age and of different (predominantly peripheral) nervous system lesions on that activity have been examined. A measurement, the %Repeater F-wave value, was devised to quantify the observed effects of lesions on the antidromically activated recurrent motor activity of motor neurone pools.

The sensitivity of the new techniques, the way in which they are best applied, their advantages and limitations, and the clinical problems they can help elucidate are all considered.

The thesis is in six parts and includes a synopsis of pre-existing data relating to the nature of the F-response and its current electrodiagnostic uses. Each of the chapters is devoted to a particular aspect of the F-response and/or its use. The chapters are sequenced so that the experiments detailed can be considered in terms of the underlying physiological mechanisms. The final chapter is devoted to the place of the F-response in the identification of lesions of the median nerve in the carpal tunnel, a commonplace clinical problem.

It is demonstrated that, in health, the motor neurone pools of different muscles, including ipsisegmental muscles, have different F-wave discharge patterns. Disorders of the peripheral nervous system (of disparate pathophysiological types; including neuronopathy and demyelinating/ axonal/compression/post-infective neuropathies) and intra-spinal lesions can modify F-wave production. The %Repeater F-wave value can be used as a readily computed index of pathological F-wave production. In some conditions it can be a very sensitive index of neural dysfunction (it may disclose abnormalities missed by conventional motor fibre nerve conduction tests) and can occur as an isolated electrodiagnostic abnormality. It is shown that by quantifying F-responses with stimuli promixal and distal to a segmental nerve lesion the lesion can be identified and localised. The latencies of F-responses evoked by motor point stimulation of abductor pollicis brevis are shown to increase the diagnostic detection rate of median nerve dysfunction in the carpal tunnel when compared with those of wrist evoked F-waves.

These experiments describe the basis for: (1) a new technique, which is an alternative to conventional velocity-based nerve conduction study techniques, for the detection and localisation of peripheral nerve lesions, (2) a new method for eliciting F responses.

INTRODUCTION

INTRODUCTION

The F-wave was described in the human by Magladery and McDougal in 1950. Uncertainty concerning its origins led, in part, to its neglect by clinical neurophysiologists until Kimura first used it to study motor impulse transmission across inaccessible nerve segments of patients with Charcot-Marie-Tooth disease in 1974. Since then, the F-wave has been used routinely in increasing numbers of clinical neurophysiology laboratories to provide data on motor fibre conduction.

Other parameters of the F-response have been considered, particularly with a view to using the F-response to quantify motor neurone excitability (Fisher 1978, Peioglou-Harmoussi et al 1985(b), Beydoun and Engel 1985). However, apart from latency measurements derived from F-response analysis no other use has, so far, been found for the F-wave in terms of diagnosing lesions of the lower motor neurone.

The inherent variability of the F-wave, as recorded from intrinsic hand muscles with a surface electrode, (another factor which initially impeded its acceptance as an electrodiagnostic measurement) might, theoretically, be turned to the advantage of the clinical neurophysiologist. It might be predicted that if the number of motor units capable of participating in the F-response fell, both the persistence and variability of the F-waves obtained from a test nerve/muscle could, in consequence, be reduced. Personal observations initially provided some encouragement and suggested that this hypothesis would be worth testing. If it proved to be correct that disorders of the lower motor neurone could result in modified F-response patterns, quantification of the F-responses issued by a test motor neurone pool might allow a new approach to the identification of a dysfunctioning peripheral nervous system.

The main objective of these studies was to find out if disorders of the lower motor neurone/peripheral nerves could alter the persistence and variability of the F-response in a way which could be quantified and used in the day to day practice of electrodiagnosis.

Initially, F-wave discharge patterns of different motor neurone pools in health were studied to determine if significant differences existed between motor neurone pools occupying similar and different spinal segments. These data were subsequently used for comparison with data obtained from patients with disorders of the peripheral nervous system. The effects of disparate peripheral nerve disorders on F-wave discharge patterns were studied using measurements of F-wave persistence and F-waveform variability. A single measurement was next devised to encompass the changes in F-wave generating behaviour observed in the unhealthy state.

Experiments were made to see how sensitive this new measurement was in detecting peripheral nerve lesions (mixed nerve entrapment) and to find out if short or long trains of supramaximal stimuli were necessary to identify lesions by quantifying a motor neurone pool's F-wave production.

Theoretically, F-discharge patterns might be more abnormal when elicited by a stimulus distal, rather than proximal, to a segmental peripheral nerve lesion. Further measurements were made to see if this obtained as such a finding would provide the basis of a new method of localising (as well as identifying) a peripheral nerve lesion.

A new method of eliciting F-responses was next considered: rather than stimulating the test muscle's mixed nerve, its motor point was stimulated. The place of this technique in the electrodiagnosis of median nerve lesions in the carpal tunnel, was considered.

The thesis is set out in a way which seeks to minimise repetition. Information pertinent to the analysis of the author's own experiments is contained in sections prior to each experiment and such information is not, generally, restated unless it is a key element in the discussion of experimental results. There are six chapters, each of which addresses a particular issue. Some speculative comments relating to the author's observations and the physiological mechanisms which might underlie these observations are scattered throughout and for economy are not, for the most part, reiterated.

In Chapter 1 an historical overview traces the study of artificially induced muscle contractions to the description of the F-wave in man. The evolution of insight into the nature of the F-response is outlined.

Chapter 2 contains a review of the latency measurements which have been derived from the F-response to date. This is followed by the author's experiments on F-wave persistence, and the persistence of identical F-waves in health. A new measurement, the %Repeater F-wave value, is introduced to quantify F-wave discharges and the influence of age on that measurement is analysed.

In Chapter 3, before possible applications of the new measurement are investigated, other "late" muscle responses which need to be distinguished from the F-response are considered.

In Chapter 4, the present electrodiagnostic uses to which the F-wave is put are reviewed, after which the influence of peripheral nerve lesions on F-discharge patterns is analysed.

Chapter 5 deals with the sensitivity of the author's method of identifying peripheral nerve lesions by quantifying F-wave production and enquires how the measurement should best be applied.

As carpal tunnel syndrome is a commonplace and important condition, a whole chapter is devoted to it. In Chapter 6, methods using the F-wave which have previously been used to identify median nerve dysfunction are reviewed. The prevalence of abnormal F-wave discharge patterns in carpal tunnel syndrome is considered and 2 new methods of identifying a segmental median nerve lesion under the flexor reticulum are described. A new clinical sign is detailed and an experiment highlighting the difficulties faced by the clinician and the electrophysiologist in correctly diagnosing "carpal tunnel syndrome" is contained. Finally, the various techniques described in the thesis have been ordered into what the author believes is an economical strategy for the electrodiagnosis of median nerve lesions, offering greater sensitivity than conventional latency-based electrodiagnostic measurements.

The methodology for evoking and recording F-responses was standardised for the experiments in Chapters 2, 4, 5 and part of Chapter 6 and, for that reason, is outlined in detail only once (see 2.2.2). In the experiment in which F-waves were elicited by stimuli delivered to the test muscles' motor point (6.9), the methodology was different and is described in detail there.

The experiments herein have all been done on human volunteers and have been conducted in accordance with medical ethical standards. Permission for the experiments was obtained from the Ethical Committee of the Tayside Health Board and informed consent was obtained from each volunteer.

Illustrations have been selected for clarity and ease of interpretation. The abbreviations S, M, F, as explained in Figure 1, are used throughout.

The observer bias implicit in the measurements made in the experiments described is discussed where appropriate.

The statistical analysis has been kept as simple as is appropriate and was done using a computerised statistical graphics system ('Statgraphics').

When the experiments of other workers are cited, it can be taken that the work refers to experiments on the human. If animal experiments (e.g. on cat) are cited, it will be made clear in the text.

Permission from co-authors and the editors of "Neurology" (Dr R.B. Daroff), "Archives of Physical Medicine and Rehabilitation" (Dr Marvin Schroder), "The Journal of Neurology", and the "Journal of Physiology" (Dr J.J. Jack) was granted to reprint the author's publications from those sources.

CHAPTER 1

CHAPTER 1

THE F-RESPONSE AND ITS NATURE

1.1. Historical Perspectives

The measurement of artificially induced muscle contractions was the starting point for the science of electrodiagnosis. It is a development of that type of measurement which forms the subject matter of this thesis.

The ancients were aware that an involuntary muscle contraction could result from contact with life forms we now recognise as capable of an electric discharge (C. Plinius Secundus). Electric current was introduced into human tissues for experimental and therapeutic purposes in the first part of the 18th century, over 100 years after William Gilbert described electricity as a force in "De Magnete, Magnetisque Corporibus et de Magno Magnete Tellure" (1600).

The invention of the Leyden jar in 1745 permitted the storage of static electricity, which, until the invention of the battery at the end of that century, was important to the expanding interest in the effects of electricity on muscle. In 1746 Kratzenstein reported an experiment in which he successfully induced muscular contractions with static electricity (Kratzenstein 1746). The origins of muscle contractions were uncertain throughout the 18th century, although Haller's observations established the fundamental principles of peripheral nerve function by the middle of the century (Haller 1756). In the preceding century physical agents, e.g. corrosive fluids and cold, rather than electric currents, had been used to induce

contractions in animal muscle (Glisson 1677). The advance towards studying the effects of nerve activation on muscle required a conceptual advance as well as a technological advance, and such a step was taken by Galvani towards the end of the 18th century (Galvani 1792). From his observations on muscle contractions in the frog he developed the view that electricity was generated in the body (so called "animal electricity") and that it originated not in muscle but in the nervous system. In 1794 he produced muscle contractions by placing the free end of a nerve across a muscle, proving that electricity could be produced by animal tissue. Although the invention of Volta's "pile" provided a reliable source of continuous electric current to physiologists experimenting on nerve and muscle, it also eclipsed, for nearly 40 years, the concept of "animal electricity" until 1838 when Matteucci proved that electrical currents could originate in muscles (Matteucci 1844).

The diagnostic use of electric current was still some way off and for decades electricity was applied to muscle for therapeutic purposes before it was used to make physiological measurements. From the mid 18th century muscular contraction induced by electricity was a therapy for paralysis and rheumatism and was even used to treat blindness (Hamilton 1835). Patients subjected to the early trials of electrotherapy were exposed to considerable risks, as not all the effects of electrotherapy could be anticipated. In Ireland, though the efficacy of acupuncture was admitted at that time, Dr John Hamilton was "not aware that it had been tried with galvanism" and reported on a trial made by Dr Stokes of the Meath Hospital which would "at least possess the merit of novelty" (Hamilton 1835). The strength of the shock used for treatments depended upon the body part being treated, the number of plates in the battery being adjusted accordingly. The necessity for caution was illustrated by Dr Stokes' experience of a patient "with some obscure chronic disease of the brain which rendered both eyes amaurotic".

"One needle was inserted just above the left eyebrow, and another at the occiput. It had been determined to commence with only 8 or 9 pairs of plates, but from a feeling of caution the circle of communication only included three pairs, and yet, with this exceedingly small number the patient was completely stunned". (Some treatments, e.g. for sciatica, involved such a battery with 50 plates).

Studies into the physiological events which follow electrical stimulation of nerve fibres outside the spinal cord derived from initial experiments on muscle physiology. In 1840 Marshall Hall used galvanic current to measure the excitability of peripheral nerves and distinguished differences in cases of paralysis resulting from central lesions compared with peripheral lesions (Mayer 1872). This is one of the earliest experiments in which the application of electricity is used to distinguish between the physiological effects of a central and a peripheral nervous system lesion. Helmholz first measured motor conduction velocity in the peripheral nerve of a frog in 1850 by recording the differences in mechanical latency in the test muscle after stimulating its nerve at two different sites (Helmholz 1850). As in the earliest experiments on muscle contractions, the first experiments on the function of peripheral nerve used mechanical, rather than electrical, stimuli. In 1658 Jan Swammerdam entertained the Duke of Tuscany, his patron, with the twitches of an isolated frog muscle, by gripping and severing its nerve: an event described in Biblia Naturae as "a most delightful and equally useful experiment" (Swammerdam [Trans.] 1758). The ability to record human action potentials was fundamental to the development of electrophysiology. Of the early experimenters with an interest in the motor system, Piper holds a place of particular importance. He acknowledged that action potentials were recorded in the last quarter of the 19th century by Bernstein, at a time when important advances in the construction of

apparatus capable of recording millivolt potentials took place (Piper 1912(a)). Before World Ward I Piper introduced a more accurate method for determining the arrival time of nerve impulses at the muscle (Piper 1908, 1912(b)). By recording the evoked potential which resulted from depolarisation of the muscle's fibres, rather than the mechanical event, he had established the basis of the technique used today for the examination of impulse transmission in alpha motor axons.

Stimulation of the proximal end of a sectioned motor root had been found to produce no contraction of the nerve's muscle as long ago as 1835 (Müller 1835), but Hoffmann later showed that centripetal impulses could be set up in a peripheral nerve which could reflexly activate muscle fibres if the integrity of the peripheral nerve was retained (Hoffmann 1918). The demonstration of human skeletal muscle being made to contract by selective activation of sensory fibres with a low intensity electric shock came within a decade of Piper's work on orthodromic motor fibre conduction (Hoffmann 1918). The capability of inducing reflex contractions in muscle has been a keystone in the expansion of understanding of both central and peripheral nervous system physiology. This work on the myotatic reflex would subsequently provide a means to study spinal reflex pathways, synaptic transmission and motor neurone excitability (Lorente de No 1938, Lorente de No and Graham 1938).

This type of experimental electrophysiology found no clinical applications until after World War II when Hodes and colleagues showed that nerve conduction velocity was slowed by a peripheral nerve lesion (Hodes et al 1948). The possibility of electrodiagnosis gaining ground as an adjunct to clinical diagnostic skills followed from the recording of nerve action potentials, first in 1937 by Eichler and then, importantly, by Dawson and Scott in 1949. Within a few years, the measurement of prolonged distal

motor latencies in peripheral nerve entrapment and the recording of pure sensory nerve action potentials obtained by electrical stimulation of the fingers signalled the beginnings of nerve conduction studies as we practice them today (Dawson 1956, Simpson 1956, Gilliatt and Sears 1958). These techniques were the cornerstones of clinical measurement of peripheral nerve function and remain so today.

The two techniques available for the study of impulse transmission in the lower motor neurone before the 1920's were augmented in the 1940's by a third technique which involved the activation of the somata of alpha motor neurones with centripetal volleys set up outside the spinal cord. It is this type of artefactual muscular contraction which will be considered in the reviews and experiments of this thesis.

At the beginning of the century the anatomical discovery of recurrent collaterals arising from the proximal axons of some human motor neurones led to speculation that discharges in some motor neurones might have inhibitory effects on others (Cajal 1909, Brown 1914). From this concept a neurophysiological investigation into the function of recurrent motor collaterals developed in the 1930's (e.g. Eccles and Sherrington 1931, Forbes et al 1933). Following from this, an important development for experimental neurophysiology, and later for clinical neurophysiology, was the use of antidromic nerve volleys in the experiments of this era (Lorente de No 1939). The concept of antidromic nerve activation was not innovative in the 1930's, indeed almost 100 years earlier attempts were made to produce muscular contractions by stimulating the proximal end of a transected motor root (Müller 1835). Other early experimenters, at the end of the last century, failed to obtain evidence of centrifugal activity in motor axons consequent upon antidromic activation (Mislawsky 1895).

It was the experiments of Renshaw which pointed to the existence of a centrifugal discharge arising in motor neurones which had been activated antidromically (Renshaw 1941). He was, at that time, interested in using antidromic activation to study the conditioning of reflex discharges of other motor neurones. Before going on to describe his findings, it would be appropriate to note the relatively advanced state of experimental neurophysiology in the 1930's and 1940's pertaining to the understanding of spinal reflexes and motor neurone excitability in comparison with the poorly developed science of electrodiagnosis. Just as electrotherapy gained ground in the 18th century well in advance of electrophysiology, some aspects of clinical neurophysiology lagged behind experimental neurophysiology in this century. Experimental work on antidromically activated recurrent motor discharges did not find a clinical application until the mid 1970's (Kimura 1974).

There are some good reasons for that failure to apply the measurement of electrically evoked "late" muscle responses to the eludication of peripheral nerve lesions, and they should become apparent as the nature of the F-response is examined later in this chapter. It will also become apparent that the application of antidromically activated recurrent motor discharges (F-waves) in clinical electrodiagnosis has not been systematically assessed.

In current electrodiagnostic practice peripheral nerve dysfunction is detected by measurements which reflect changes in conduction velocity, whether by measuring conduction velocity in a single motor unit or by quantifying reductions in the size of evoked sensory nerve or compound muscle action potentials. The applications that the F-response has found in clinical neurophysiology will be dealt with in detail in subsequent chapters (Chapters 2, 4, 6). Essentially, F-responses have been used to provide

sensitive measurements of impulse conduction in largest and fastest conducting alpha motor neurones along their full length or over proximal nerve segments, inaccessible to conventional techniques (Kimura 1974, Kimura and Butzer 1975, King and Ashby 1976, Shahani et al 1987). The determinants of a motor neurone pool's F-wave discharging behaviour have not received much attention and our understanding of them is very incomplete. The influence of peripheral nervous system lesions on the patterns of recurrent motor discharges obtained in response to trains of antidromic volleys has not been assessed, and it is a study of this which forms the bulk of the experimental work contained in this thesis. Before considering the effects which peripheral nervous system lesions might have on F-wave discharges, it is necessary to examine the nature of these neurophysiological artefacts.

1.2. The Original Observations on Recurrent Motor Discharges in the Cat

Renshaw was interested in the physiological implications of Cajal's anatomical observations (Cajal 1909, Renshaw 1941). He supposed that activity in a motor axon must invade its collateral branches and asked whether the excitability of neurones with collateral terminals on them was consequently affected. One of his aims was to assess the conditioning effect of antidromic activation of certain groups of motor neuornes on reflex discharges of other motor neurones. In the course of these experiments he recorded low amplitude, delayed, centrifugal discharges which appeared intermittently in motor axons in which he had set up an antidromic volley. The experimental model he used in these studies was an anaesthetised cat in which the ventral rootlets of the 7th lumbar segment had been divided into two equal groups. He found that an antidromic volley in either group of rootlets resulted in a centrifugal impulse in some fibres of the same rootlets. He characterised these responses and made some perceptive deductions based on his own observations. Most importantly, the delayed response he obtained, after antidromic activation of the motor neurone pool, could be recorded only from axons which conveyed the centripital volley. He found that stimulation of the large mixed peripheral nerve of the hind limb, at a distal site, provoked a similar late response to that obtained by root stimulation and that the latency of the response was proportional to the distance of the stimulus and recording sites from the spinal cord. The "late" responses could be recorded from nerves to individual muscles of the leg. The genesis of this centrifugal discharge was dependent on the integrity of the spinal cord but was independent of the orthodromic sensory volley set up concomitant with the antidromic motor volley in a mixed nerve, as it was possible to generate these potentials after section of the relevant dorsal roots. He observed reversible abolition of these "late" responses during

subtotal spinal cord asphyxia. The efferent discharge was found, consistently, to be small in comparison to the antidromic volley and occupied a small fraction of nerve fibres transmitting the centripetal volley. He also found that the efferent discharge could be conditioned by a preceding dorsal root volley. As to the origin of the response, Renshaw believed that synaptic excitation of motor neurones by antidromic volleys conducted through recurrent collaterals was improbable. This was in spite of the calculated central latency of the response being equivalent to the synaptic delays at motor neurones previously determined by Lorento de No (1938). Renshaw computed a central latency of Ca. 0.9 ms (assuming fastest fibres conveyed the impulses) by subtracting the conduction times in the motor axons of the centripetal and centrifugal impulses from the total latency of the response. Because the late responses appeared only in motor fibres transmitting the antidromic volley, he suggested that the centrifugal discharge arose from "repetitive activity" in a small number of antidromically activated motor neurones. The antidromic volleys he used, while capable of conditioning reflex discharges into other motor neurones, never set up centrifugal discharges in motor neurones other than those transmitting the antidromic impulses.

1.3. Identification of the F-wave in Man

A decade elapsed after Renshaw's work on cats before the first significant paper appeared with observations on a similar type of response in man.

Magladery and McDougal (1950) noted that when an electrical stimulus to a mixed nerve was suprathreshold for motor axons a small, but distinct, potential could be recorded from intrinsic hand and foot muscles following the direct motor response. They named this deflection on the oscilloscope the F-wave. It varied in prominence in different subjects and required variable levels of amplification to be apparent when the recording was made with surface electrodes. Figure 1 shows the typical variability of latency and waveform encountered in the F-responses recorded from a train of stimuli applied to abductor pollicis brevis in a healthy adult (Figure 1). Unlike Hoffmann's reflex (termed the H-reflex by Magladery and McDougal) it did not diminish in size with increasing stimulus intensities. As antidromic motor activation occurred in conjunction with orthodromic sensory conduction with the stimulus strengths they were applying to elicit the F-response, they tried to determine if it was an antidromically activated central discharge of motor neurones or a true reflex response. In view of the F-wave's failure to diminish with high intensity shocks, they proposed it could be a reflex with a slowly conducting afferent limb. It was suggested that if the centripetal impulses subserving the response were more slowly conducted than impulses in the fastest motor fibres, then motor neurones would be able to transmit the reflex response having recovered from the antidromic motor volley. Having established that the latency of the F-response could be shortened by moving the stimulus on the mixed nerve nearer to the spinal cord, they determined to measure the conduction velocity in the afferent limb of the F-response by stimulating at two

FIGURE 1

F-waves recorded from the abductor pollicis brevis of a healthy adult showing the typical variability in latency and waveform.

S = stimulus artefact
M = M wave
F = F-response

separate sites on the nerve and measuring the distance and latency between the two. If fastest motor axons conducted the centripetal impulses involved in the F-response the latency difference (and conduction velocity) between the two sites of stimulation would be identical to that of the M wave recorded from those two sites. They found, as they had predicted, that the conduction velocity in the afferent fibres transmitting the F-wave was approximately 10 m/s slower than in those fibres conducting the M wave over the same length of mixed nerve. This led them to conclude that the F-wave had a reflex origin mediated by slow conducting afferents.

Evidence from other investigators has subsequently been incompatible with this view and will be discussed later. The important observations which Magladery and McDougal made on the F-wave included those on its anatomical distribution in upper and lower limb muscles, its latency and its retention in patients in whom tendon reflexes and H-reflexes were absent. The F-wave could only be recorded from muscle innervated by the stimulated nerve and, unlike the H-reflex, was easily recorded from upper and lower limb musculature including the territories of the median, ulnar, peroneal and posterior tibial nerves. The configuration and latency of successive F-responses, when recorded from an individual muscle under stable conditions of stimulation, were inconstant. In any ulnar innervated intrinsic hand muscle, however, the F-response fell in a narrow latency range, earliest and latest conducted responses being separated by no more than 2 ms when the stimulus was applied to the ulnar nerve at the wrist. When recorded from the hypothenar eminence, stimulating at wrist level, F-waves with latencies of approximately 31 ms were recorded. Evidence that propagation of impulses occurred in a central direction to produce the F-wave was found by abolition of the response by a procaine nerve block sited proximal to the stimulus. This work stimulated an interest in this "late" motor

response which had been recorded incidentally, and disregarded, by other workers (Dawson and Scott 1949).

1.4 On the Nature of the F-response

1.4.1. A reflex or a recurrent motor discharge?

Hagbarth speculated that the F-response might be a rudimentary H-reflex in the intrinsic hand and foot muscles whence an H-reflex can be recorded in infancy (Thomas and Lambert 1960, Hagbarth 1962, Hodes and Gribetz 1962) or in the presence of a pyramidal tract lesion (Teasdall et al 1952). The F-response recorded from thenar muscle can be converted into a response with the characteristics of the monosynaptic reflex by tetanization of the median nerve (Hagbarth 1962). In Hagbarth's experiments the reflex which appeared in the post-tetanic period resulted from a number of identifiable and separate effects. The rise in stimulus threshold of motor axons and the presynaptic potentiation induced by a tetanus diminished steadily with time in the post-tetanic period and a gradual transition of the H-reflex back to an F-response was observed with stimuli which had been subliminal for motor fibres in the early post-tetanic phase. These experiments using a tetanus did not allow any definite conclusions on the nature of the F-wave, but did promote the concept of the F-response as a reflex partially obliterated by the antidromic motor volley.

Magladery and McDougal (1950) used measurements of the conduction velocity in the afferent limb of the F-response to determine if the response was a reflex or represented a recurrent motor discharge. Those results, which were interpreted as giving evidence in favour of a reflex mechanism, conflict with data from later studies in human subjects, in particular, with data obtained using the single fibre EMG method to study antidromic and orthodromic conduction in single motor units transmitting F- and M responses (Dawson and Merton 1956, Thorne 1965, Mayer and Feldman 1967, Trontelj and Trontelj 1973).

Contradicting the earlier findings of Magladery and McDougal, Dawson and Merton (1956) calculated the fastest conduction velocity in motor axons and in fibres transmitting minimal latency F-waves over the same long segments of the ulnar nerve and found them to be identical. Elsewhere, studies were done on patients with lower lumbar and sacral spinal root dysfunction in whom the soleus H-reflex was absent. This showed that the centripetal F-wave conduction velocity (from the earliest F-wave) in the ankle to knee segment of the posterior tibial nerve was the same as the fastest motor conduction velocity in the same nerve segment (Mayer and Feldman 1967). In patients on whom dorsolateral longitudinal myelotomy had been performed for the relief of spasticity, antidromic and orthodromic conduction latencies in the fibres transmitting the F-response have since been found to be identical (Miglietta 1973).

In view of the opposing concepts which derived from the work cited, a new approach was required to illuminate the nature of the F-response. Hagbarth's view that the F-wave might represent a rudimentary H-reflex lacking pre- or post-synaptic facilitation and/or partially blocked by the antidromic motor volley was not supported by Thorne's experiments on the single motor unit composition of the M wave and F-wave (Thorne 1965). Use of an EMG needle with a small recording volume allowed the identification of isolated single motor units, or single motor units in small groups, in the direct motor response (M wave). The test nerve was excited electrically through the skin and once the test motor unit(s) in the M response of the test muscles was (were) identified a comparison of the single motor unit composition of the F-wave and the M wave could be made. The stimulus was adjusted to activate single or small numbers of motor units in the territory covered by the needle electrode's recording volume. At no time was a motor unit recorded from the F-reponse which was not represented in the M wave.

Characteristically, an F-response in a single motor unit followed that unit's M wave only infrequently. Depending on the intensity of the stimulus, and the position of the stimulating electrode in relation to the nerve trunk, different motor units could be identified in the M wave and these motor units were seen to appear singly or in various combinations in the F-wave. Thorne also noted an absence of post-tetanic potentiation of the F-response and suggested this observation as indirect evidence for a mode of genesis different from that of the monosynaptic and polysynaptic reflexes. These experiments on the single motor unit composition of the M and the F-response supported the concept that the F-response resulted from recurrent discharges in a variable fraction of the test motor neurone pool as was suggested by Dawson and Merton (1956).

Another strand of evidence which supported the view that the F-wave resulted from recurrent motor discharges came from studies on deafferented limbs. These studies showed that generation of the F-response could occur independent of sensory inputs through the dorsal roots (Magladery and McDougal 1950, Thorne 1965, Mayer and Feldman 1967, Miglietta 1973, Fox and Hitchcock 1985). "Late" responses with the same characteristics as the human F-wave can be recorded from the hand of the baboon and the close anatomical resemblance of the forelimb of the baboon to the human upper limb suggested its use to study the effects of experimental deafferentation on F-waves (McLeod and Wray 1966). Section of the C5-T2 dorsal roots at the zone of entry to the spinal cord failed to abolish ipsisegmental F-responses, indicating their source in the lower motor neurone. As in the baboon, the human F-response has been conducted in the absence of an afferent pathway for a reflex discharge. Mayer and Feldman (1967) recorded F-responses, with their typical characteristics, from the hypothenar eminence of a patient who had been surgically deafferented between the level of

C7-T1 as a treatment for intractable pain. (The afferent and efferent fibres which innervate the hypothenar muscles are conveyed mainly from the C8 and T1 roots with a lesser representation in the C7 root). Previously, F-responses had been found intact in patients with congenital sensory neuropathy and tabes dorsalis, but these reports, while of interest, failed to provide definitive evidence of the mechanisms underlying the F-response (Thorne 1965). The procedure of dorsolateral longitudinal myelotomy carried out for the relief of spasticity in the lower extremities is designed to retain connectivity between the pyramidal tracts and the motor units they govern, while reducing sensory inputs which impinge on the anterior horn cells and maintain spasticity. Miglietta (1973) demonstrated that after this procedure the F-response could still be recorded from intrinsic foot muscles when clonus was abolished and an H-reflex could no longer be recorded from calf muscle.

Definitive studies on the nature of the F-response have utilised single fibre EMG techniques and these have supported the concept derived from the F-wave velocity measurements of Dawson and Merton and the single motor unit studies of Thorne.

A single fibre EMG electrode permits the isolation of the action potential(s) of one or several muscle fibre(s) in a single motor unit from those of the entire unit population (Ekstedt et al 1969). To study "late" responses in an individual motor neurone its muscle fibres' action potentials are identified by their characteristic shape, amplitude and duration. Identification of activity in a single motor neurone is most readily accomplished when the recording is made from 2 or more of the muscle fibres of its motor unit as evidenced by the all-or-none appearance of the whole complex of potentials. Variations in the onset of a single muscle fibre's action potential evoked by consecutive stimuli can be accurately

timed and this allows distinctions to be drawn between "late" responses of different origins e.g. reflex or recurrent motor responses. The jitter of the F-response exceeds that of the preceding direct motor response in the same muscle fibre only slightly (Trontelj and Trontelj 1973) and is incompatible with a reflex mechansism (Schiller and Stålberg 1978). There is a considerable variation in the latency of successive H-reflex responses of single motor neurones (e.g. >400 µsec) of triceps surae while the F-wave jitter in abductor digiti minimi is Ca. 40 µsec (SD 10 µsec) (Trontelj 1973, Schiller and Stålberg 1978).

The jitter of the F-response is probably due to additional variable delays in impulse propagation at a number of different sites other than the neuromuscular junction e.g. at nodes of Ranvier, at the axon-soma and soma-axon junctions (Stålberg et al 1973). In the motor neurones of the facial nerve the M wave jitter has been measured at Ca. 37 µsec, while in the same population of motor units the F-response jitter was Ca. 48 µsec (equivalent S.D. values) (Trontelj and Trontelj 1973). The jitter value of the F-response is approximately 20% higher than the M wave jitter in the same motor neuorne (Stålberg et al 1973).

Single fibre EMG allows a recurrent discharge to be distinguished from a reflex discharge in a motor neurone not only through measurements of jitter but also by detecting the presence or absence (respectively) of a preceding M wave of an identical configuration and amplitude.

It has been suggested that "late" muscle potentials recorded from the frontalis muscle when stimulating the facial nerve electrically must, necessarily, represent recurrent motor neurone activity as the facial nerve contains no afferent fibres (Sawhney and Kayan 1971). However, single fibre EMG electrode studies have shown that reflex potentials can be recorded from the muscles of facial expression after stimulating the facial nerve

electrically (Trontelj and Trontelj 1973). Positioning the stimulating electrode out of range of the facial nerve and recording from the facial nerve's musculature it can be shown that reflex components probably arise from inadvertent stimulation of trigeminal sensory nerve branches. These reflex potentials, transmitted by individual motor neurones, have been shown to have latency variations with consecutive stimuli appropriate for transmission in a polysynaptic pathway (Trontelj and Trontelj 1973). Another distinct type of "late" response,with a much shorter latency, can be recorded by single fibre EMG from single motor neurones in orbicularis occuli and orbicularis oris stimulating the facial nerve extracranially (Trontelj and Trontelj 1973). By varying the intensity of the stimulus it has been shown that this response is invariably preceded by a direct M wave in the same motor neurone and follows less than 5% of M responses. In double pulse experiments a consistent temporal relationship of the M wave to the F-response was found in single muscle fibres of individual motor neurones. When the stimulus strength was near the threshold for the direct response the "late" response never occurred if the direct response failed, indicating that the "late" response required direct activation of the motor axon.

These studies are the most definitive illustration of the nature of the F-response. They allow identification of an individual motor neurone conducting the impulses which depolarise an individual muscle fibre, directly and recurrently, and permit observations on the variations in latency incurred when the impulse is transmitted from the peripheral stimulus site to the spinal cord and back to the recording site in muscle.

Single fibre EMG jitter measurements of serial F-responses provide a measure of the narrow temporal window through which an individual motor neurone's F-response can be conducted. This observation will be returned to when the subpopulation of alpha motor neurones in each test motor neurone

pool participating in the F-response is considered (see 1.4.3, 4.2.1).

The most detailed and informative study on impulse conduction in the afferent and efferent pathways transmitting the F-response was also done by Trontelj and Trontelj (1973) who produced unexpected results when they calculated the orthodromic and antidromic conduction velocities of F-responses recorded from single muscle fibres supplied by the facial nerve. These F-responses were defined by a number of parameters and were clearly shown, through single fibre EMG techniques, to represent recurrent motor discharges (see above). Between two stimulation points on the facial nerve (one at the stylomastoid foramen, the other at the margin of the orbit) differences in the recorded M and F-wave latencies in single motor neurones showed antidromic conduction to be consistently more rapid than orthodromic conduction in individual axons (by up to 4.7 m/s). The discrepancy between the values for conduction latencies in the afferent and efferent pathways of the F-response was explained by an experiment with paired stimuli in which a second direct response (timed simultaneously with the F-response evoked intermittently by the first stimulus) was transmitted more rapidly than the first direct response. It is possible, therefore, that each direct response (M wave) was followed by a supernormal period when increased propagation velocity along the muscle fibre shortened the "late" response latency. In keeping with this explanation the shortening of the F-response latency was found to be greatest when the stimulus was moved proximally.

1.4.2. F-wave discharge patterns of single motor neurones

It is known that F-responses evoked in individual motor neurones supplying the facial muscles follow the M response infrequently (Trontelj and Trontelj 1973). Quantitative experiments on F-wave persistence in single motor neurones have been reported only in healthy abductor digiti minimi muscles to date (Schiller and Stålberg 1978).

Schiller and Stålberg identified F-responses in single motor neurones using a single fibre EMG electrode, and in long duration experiments, the F-response frequency (or F-wave persistence) in single motor neurones has been determined over periods of up to 45 minutes. In these experiments stimuli were delivered at 1 or 2 Hz. The F-responses in individual motor neurones were unevenly distributed in time and tended to appear in clusters. The results of this experiment will be outlined in some detail as they have particular relevance to the interpretation of results of the author's experiments which follow. During periods of stimulation equivalent to 600 M waves, (10 minutes at 1 Hz), no F-responses could be recorded in some test hands. When a burst of F-responses did occur they could follow consecutive stimuli, although the majority did not. Additionally, large numbers of individual motor neurones were studied in healthy subjects with a shorter period of stimulation yielding 200 M waves. In the course of this experiment 55% of motor neurones generated no F-responses, 35% generated 1-5 responses and 4% between 5-10 responses. No test motor neurone transmitted more than 15 F-responses per 200 M waves. The average rate was 1 F-wave per 118 M waves.

The information obtained on F-wave persistence from a single fibre EMG needle and a surface recording plate is very different. When recorded with a surface electrode, the action potentials from motor unit territories of single or small numbers of motor neurones may not be detected (Yemm

1977). It is uncertain, at present, if a supramaximal motor nerve stimulus is invariably followed by some (albeit undetected) recurrent discharges. In their studies on F-wave persistence in single motor neuornes, Schiller and Stålberg used stimulus intensities which were suprathreshold for the M wave of the motor unit under scrutiny. Importantly these test shocks would have been subliminal for most of the test nerve's motor axons and did not reproduce the conditions which obtain when F-responses are evoked conventionally (Thorne 1965). In this experiment, the possible bias towards and against activation of motor units with certain characteristics is of interest. Traditionally, it would be expected that weak electrical stimuli to a peripheral nerve would depolarise large rather than smaller axons. However, it may be that the anatomical arrangement of axons in a mixed nerve is relevant to observations that this prediction is not fulfilled (Kadrie et al 1976). However, it is clear that the majority of motor neurones fail to discharge an F-response when an impulse is conducted antidromically into any test motor neurone pool (Thorne 1965, Eisen and Odusote 1979, Fisher 1978). Usually <5% (and most commonly Ca. 1%) of a test muscle's compound action potential can be generated by a recurrent motor discharge at any given moment (Fisher 1978, Eisen and Odusote 1979, Kimura et al 1984). This aspect of the F-response, with reference to the fraction of the motor neurone pool (in terms of motor unit numbers) which can be activated at a given moment, will be discussed more fully in an introduction to the author's observations on Repeater F-waves and F-wave persistence (see 2.2, 2.3) and also in the section on motor neurone excitability (see 4.2.1).

The varying patterns of persistence of F-responses observed in individual motor units are intriguing and alterations from the normal will be described in the experiments which follow. The effects of a cortico-spinal tract lesion on individual motor neurones' liability to discharge an

F-response will be discussed in Section 4.2.1.

Yates and Brown (1979) failed to demonstrate an anticipated relation of a single motor unit's surface voltage to the latency of its recurrent discharge (Kadrie et al 1976).

1.4.3. The effects of voluntary contraction and tetanization of a muscle on the "late" responses recorded from that muscle

The F-wave evoked by a supramaximal nerve stimulus and recorded from a resting muscle can be modified by synchronising the test stimulus with a maximal voluntary contraction of that muscle (Upton et al 1971). The "late" response which occurs under these conditions arrives at the muscle approximately 2 milliseconds earlier than the F-wave when elicited from abductor pollicis brevis, (with the stimulus at the wrist), and has a considerably enhanced amplitude. Hagbarth found that an F-response can be turned into an H-reflex in lower limb muscle (e.g. tibialis anterior), as well as in thenar muscle during voluntary contraction of a test muscle (Hagbarth 1962). Under these conditions, an electrical shock of an intensity less than that required to maximise the M wave's amplitude shortened the latency of the "late" response. In Hagbarth's experiments a slight or moderate voluntary contraction was used to enhance the reflex component which was abolished by the application of a supramaximal nerve stimulus. The "late" response obtained with a supramaximal stimulus during the same degree of voluntary muscle activity was several milliseconds later than the reflex component obtained with a submaximal stimulus, i.e. the "late" response regained the latency and amplitude of the F-response obtained at rest.

The experiments of Upton and his colleagues utilised a maximal willed contraction of the test muscle which resulted in the production of different types of late responses from that obtained in the resting state when a supramaximal stimulus was applied to the test nerve (Upton et al 1971). Following the M wave they recorded a response which they termed V1

which was followed, in turn, by a second response which they called V2 (at 50-60 milliseconds in abductor pollicis brevis). V2 can be recorded less consistently than V1. Dorsal rhizotomy experiments show that the integrity of ipsisegmental afferent transmission is essential to the genesis of these responses. The fluctations in V1's amplitude, observed when stimulus intensities are varied, are typical of those seen in the H-reflex of soleus at rest (Schieppati 1987).

The "clearing" of motor axons for reflex conduction after collision between antidromic and volitional impulses is likely to be an important aspect of recording a potential with the characteristics of an H-reflex from the thenar muscle utilising a shock which is supramaximal for the M wave. Facilitation of motor neurones is likely to be important in the recording of H-reflexes from the hand muscles. As well as voluntary contraction in abductor pollicis brevis producing facilitation of its motor neurones, the formulation of the desire to contract the muscle has a similar facilitating effect and can allow V1 to be recorded prior to the onset of the willed contraction (Upton et al 1971). In addition to the effects which a muscle contraction has on the liability of a reflex discharge to be recorded from that muscle, the contraction also influences the liabilities of the neurones of the test motor neurone pool to issue a recurrent response. The effects of a contraction on the depolarisation/repolarisation schedules of the axon-hillock - soma region in health will not be discussed here. The reader is referred to section 4.1.12 where this is considered.

Voluntary contraction of a test muscle is used in some EMG laboratories to increase F-wave persistence and amplitude when recording F-waves to make latency measurements (e.g. Massachusetts General Hospital, Boston). This practice has been avoided in the experiments which follow.

The fraction of the test motor neurone pool which discharges an F-wave in response to a single shock can also be modified by contraction of contralateral ipsisegmental muscles. Voluntary contraction of the abductor pollicis brevis contralateral to the abductor from which F-waves are being recorded produces cross facilitation of test motor neurones (Knezevic et al 1985). This effect is influenced by fatigue and with the cessation of contraction there is a rebound depression of motor neurone excitability. F-responses recorded from abductor pollicis brevis when the contralateral muscle is contacted increase in persistence, amplitude and complexity. This effect is, in part, independent of a facilitation of reflex activity. Following deafferentation of thenar muscle and tibialis anterior by dorsal root section (C5-T2 and L3-S5 respectively) voluntary muscle activation can still be associated with a statistically significant increase in F-wave amplitude. This finding is compatible with an upper motor neurone effect on the readiness with which motor neurone somata issue recurrent discharges (Fox and Hitchcock 1985).

V1 and V2 were recorded by Upton and colleagues (1971) using supramaximal nerve stimuli. A relatively weak electrical stimulus which preferentially activates large diameter, low threshold, afferent fibres and fails to activate the majority of higher threshold motor fibres, when applied to the median nerve, will produce no reflex response in the normally innervated and relaxed adult abductor pollicis brevis muscle. That same stimulus applied during a willed contraction of abductor pollicis brevis evokes two temporally related reflex potentials. Eisen and colleagues (1984) found that a stimulus of an intensity which produced an M wave, with an amplitude no greater than Ca. 100 μV, was appropriate for recording these "late" responses which they named R1 and R2. These responses can be recorded from tibialis anterior by stimulating the peroneal nerve and, as

with those from abductor pollicis brevis, moving the stimulus proximally shortens their latency. The latency of R1 from abductor pollicis brevis, with the stimulus to the median nerve at the wrist, is similar to that of the F-wave. It is, however, necessary to average large number of responses to obtain clear recordings of R1 and R2, particularly the latter. R2 from abductor pollicis brevis can be maximised by stimulating the superficial radial nerve and this finding has suggested that R2 is mediated by fast conducting fibres other than Ia muscle afferents (Eisen et al 1984).

Post-tetanic potentiation of the monosynaptic pathway has been demonstrated in animals (Lloyd 1949, Eccles and Rall 1951). These experiments showed no increased excitability of motor neurones, as tested by an antidromic volley after tetanization, suggesting that the enhancement of reflex activation was due to a change confined to the presynaptic pathway. This hypothesis was later supported by the work of Wall and Johnson (1958). Post-tetanic potentiation has since been demonstrated in human calf muscle using the monosynaptic reflex (Hagbarth 1962). The absence of post-tetanic potentiation of the F-response in normal subjects is compatible with a mode of production different from mono- or polysynaptic responses. Intense tetanic stimulation of motor axons produces a post-tetanic depression of the M wave in man (Hughes and Morrell 1957), the origin of which lies in an elevation of threshold for electrical stimulation (Hagbarth 1962). Using hypothenar muscles, Hagbarth showed that in the post-tetanic period, stimuli which had an intensity just adequate to evoke a maximal M wave pre-tetanization, evoked a "late" response typical of the H-reflex (i.e. higher in amplitude than the M wave and blocked by supramaximal stimuli). As the post-tetanic effects waned, if the same stimulus was applied there was a gradual regrowth of the M amplitude and a reduction of the reflex component which returned to having the hallmarks of an F-response. These

changes in the nature of the late deflection throughout the post-tetanic period could not be demonstrated when a stimulus supramaximal for the M wave was applied.

These various findings illustrate that, by modifying the excitability of the motor neurone pool, the excitability of motor fibres in the peripheral nerve and the level of antidromic activity in motor fibres, "late" responses with reflex characteristics can replace the F-wave. Notably, stimuli of an intensity supramaximal for the M response during the post-tetanic period ablate "late" components with reflex characteristics.

CHAPTER 2

CHAPTER 2

F-WAVE PARAMETERS AND THEIR MEASUREMENT

2.1. Measurements Derived from F-wave Transmission Times

2.1.1. Introduction

Surface recorded F-responses can be used to examine conduction latency or velocity in groups of fast conducting motor neurones along their full length or across specific segments, particularly those which are inaccessible to surface stimulation (Shahani et al 1987). The first section of this chapter is concerned with the measurements which have, so far, been made from F-responses for electrodiagnostic purposes. The various applications found for these measurements, to date, will be described separately in Chapter 4. Some difficulties implicit in the use of these measurements will be noted. The remaining 3 sections (2.2, 2.3, 2.4) contain the author's observations on F-wave persistence and the persistence of identical F-waveforms in health. A measurement, which can be used to characterise the F-response pattern of a motor neurone pool, is described.

2.1.2. Motor conduction to and from the spinal cord

The latencies of F-responses recorded by surface electrode from an individual muscle vary from one stimulus to the next in the healthy state and the latency range of those responses which appear earliest (the range of minimal latencies) can be measured accurately only if large numbers of

responses are recorded (Panayiotopoulos and Scarpalezos 1977, Panayiotopoulos et al 1977, Panayiotopoulos 1979, Peioglou-Harmoussi et al 1985(a)). This variability in F-response latency was one factor which probably impeded the earlier incorporation of F-wave measurements into electrodiagnosis. In fact, it turns out to be a strength of the F-wave, in that it provides an extremely sensitive measure of conduction in the fastest alpha motor axons (Trontelj and Trontelj 1973, Panayiotopoulos and Scarpalezos 1976(a), Panayiotopoulos 1979, Lachman et al 1980, Shahani et al 1987). The latency range of earliest appearing F-waves in a muscle (F chronodispersion) (recorded with a surface electrode and evoked with a supramaximal stimulus) does not, of course, represent the full spectrum of F-response latencies of the individual motor neurones participating in the recorded F-response as the antidromically activated discharges which travel in slower conducting axons will be obscured by the late phase of the fastest transmitted discharges (Kimura et al 1984, Shahani et al 1987). In F chronodispersion studies of the healthy deep peroneal nerve Panayiotopoulos (1979) found maximum to minimum F-wave latency differences of up to 7.5 msec recorded from extensor digitorum brevis and noted that there was an inconstant distribution of F-wave latencies within the latency range; e.g. in one nerve/muscle more than 50% of F-waves (of 100 recorded) had latencies near the minimal value, while in another nerve it was less than 10%. The popular practice of measuring 10, or so, F-response latencies (e.g. EMG Laboratory, Massachusetts General Hospital, Boston, Mass.) is attended by a significant risk of omitting the fastest conducted F-wave (Peioglou-Harmoussi et al 1985(a)). For the purpose of estimating proximal segment motor conduction latencies and velocities the minimal recordable F-wave latency can be used and is assumed to represent centripetal and centrifugal transmission in the same group of fastest conducting motor fibres as conduct the earliest

components of the M response (Dawson and Merton 1956, Thorne 1965, Trontelj and Trontelj 1973, Kimura et al 1984, Shahani et al 1987). The F-response can be evoked from any accessible point along the course of the motor nerve but can be distinguished from the M response only if the two are sufficiently separate in time; this is dependent on the length of the lower motor neurones from the spine to the muscle, the motor fibres' conduction velocities, the site on the nerve at which the electrical stimulus is applied and the duration of the M wave. The F-wave is readily identified in hand, foot, calf and distal forearm muscles stimulating (respectively) the median, ulnar, posterior tibial, deep peroneal, superficial peroneal, anterior interosseous and posterior interosseous nerves at wrist, ankle, knee and forearm level.

The latency of the F-wave represents the transit time of the motor impulse to and from the spinal cord, and for diagnostic purposes, a number of methods based on F-wave latency analysis can be used by the clinical neurophysiologist to determine whether lesions affect the test motor nerve diffusely or at one or more circumscribed sites. Measuring conduction latency over longer segments of nerve than are conventionally tested in motor nerve conduction studies allows the identification of relatively mild slowing which can otherwise go undetected (Lachman et al 1980). To obtain a latency for transmission across a proximal motor segment of the ulnar and median nerve a stimulus can be applied at the axilla and the F-responses recorded from an appropriate intrinsic hand muscle (Baba et al 1980). This gives information on motor conduction through the brachial plexus, the C8/T1 motor roots, and the intraspinal portion of these lower motor neurones. The F-response recorded in this way is normally buried in the M response but can be isolated by employing a collision technique wherein two nerve stimuli are applied simultaneously, one at the axilla and one at the

wrist (Kimura and Butzer 1975, Kimura 1976(a)). The orthodromic impulses from the axilla collide with the antidromic impulses from the wrist leaving the wrist-evoked M response and the axilla-evoked F-response intact and distinct. From this a latency can be calculated for fastest conducted motor fibre impulses in the axilla-spinal cord segment.

Motor conduction velocities calculated across a length of nerve can give misleading information in the presence of conduction block if it selectively involves fastest conducting fibres and spares the slower conducting ones. A similar problem complicates the interpretation of central motor conduction latencies obtained from M and F-wave measurements. Central motor conduction latency has been estimated using the simple formula (F -M -1)/2 (ms), where F and M are latencies of the earliest of a series of F- and M responses evoked from the same stimulus site and 1 ms is taken to be the central delay at the anterior horn cell (Kimura 1974). The exact central delay which occurs when an antidromic impulse backfires a motor neurone is unknown, but the absolute refractory period of the fastest motor fibres lasts approximately 1 ms (Kimura 1976(b), Kimura et al 1978). The "turnaround" time for an antidromic impulse in each anterior horn cell in a test motor neurone pool will relate in part to the size of the cell body and the use of an unproven unvariable figure for the central delay in F-wave genesis is open to criticism (Young and Shahani 1978). A block of fast conducting motor fibres proximal to the nerve stimulus may result in F-responses appearing only in slower conducting fibres giving the misleading impression of slowed conduction proximally. In practice, the identification of dysfunction in the proximal segment of motor fibres is adequate for most diagnostic purposes and the ability to distinguish between conduction block and slowed conduction in fastest motor fibres is not always essential. To determine if an F-response with a pathologically prolonged latency is being

conducted in fibres with identical (or near identical) conduction characteristics to those transmitting the earliest component of the M wave orthodromically at a normal conduction velocity (i.e. normal distal segment fastest alpha axons), the sums of the F- and M latencies evoked at distal and proximal sites can be compared.

An important use of the F-wave is in measuring motor nerve conduction between the axilla and spinal cord, a length of nerve inaccessible to conventional techniques (Kimura 1974). Kimura's work in the 1970's introduced a new dimension to electrodiagnosis; the capability to study impulse transmission in proximal motor segments. It also marked the start of an acceptance of F-wave measurement into clinical neurophyisology laboratories worldwide. To obtain a prediction of F-wave conduction latency from the axilla to the test muscle there is an alternative to the collision technique already mentioned. (It should be noted that this method provides only an estimate (for reasons see below)). Making the assumption that the F-wave recorded with the minimal latency is transmitted across the axilla-cord segment in the same motor fibres that conduct fastest M wave impulses orthodromically from the axilla to the muscle, F-wave latency from the axillary stimulus site to the muscle in the hand can be estimated by subtracting the latency of the M wave evoked at the axillary site from the total of the F- and M wave latencies obtained at the wrist; i.e. F(A) = F(W) +M(W) -M(A). (F and M(A) = F- and M responses' latencies evoked by the axillary stimulus, F and M(W) = F- and M responses' latencies evoked by the wrist stimulus (Baba et al 1980). An axilla-cord-axilla F-wave latency prediction can be made from the same measurements by modifying the subtraction to take account of afferent and efferent distal transit time. Kimura and Butzer (1975) have found, in patients with the Guillain-Barré syndrome, that the F-wave conduction velocity in the antidromic direction

and the orthodromic motor nerve conduction velocity are identical over the same segment. The differences in motor conduction in the afferent and efferent limbs of the F-response in single motor neurones found by Trontelj and Trontelj (1973) have already been alluded to.

2.1.3. F-wave latency

F-wave latency can be measured from the initial deflection of the earliest or the latest appearing F-wave from a series of responses, as a latency range, or as a latency mean (Panayiotopoulos 1979, Lachman et al 1980, Fisher 1982). Unless the test subject provides a comparable nerve/muscle as a control measurement (and there are difficulties associated with this, particularly in tests for carpal tunnel syndrome) any F-wave latency measurement has to be related to nerve length and the subject's age by comparison with an appropriate set of control values and recording techniques have to be standardised for purposes of comparison (Conrad et al 1975, Weber and Piero 1978, Lachman et al 1980, Peioglou-Harmoussi et al 1985(a)). There is a strong correlation between minimum and maximum F-wave latency and height while the relationship with age (an increase in latency with increasing age) is much weaker (Conrad et al 1975, Peioglou-Harmoussi et al 1985(a)). A multiple regression equation can be used to predict F-wave latency values from an individual's height and age (Weber and Piero 1978). Kimura quotes normal values for his laboratory as mean + 2 S.D. of a large control group without allowing for height variation (Kimura 1983). This practice results in a reduction in the sensitivity of latency measurements and causes difficulty in the interpretation of F-wave latency values from unusually tall subjects.

Although the minimal F-wave latency can be abnormal while the other conventional parameters tested in nerve conduction studies remain unaffected by nerve entrapment or peripheral neuropathy (Egloff-Baer et al 1978, Lachman et al 1980), mean F-wave latencies can, in some cases, show a conduction defect more clearly (Fisher 1982)

A technique employing F-wave latency which obviates the need to compare values of a test nerve with values obtained from height and age matched control subjects uses the latency difference between the earliest F-response of the test nerve and that of another nerve in the same limb. This is particularly useful in median nerve entrapments when the contra-lateral median nerve may be damaged producing prolongation of F-wave latencies without any symptoms (see 5.3). In 103 healthy hands Egloff-Baer and colleagues (1978) found that the latency difference between the earliest F-responses recorded from abductor pollicis brevis and abductor digiti minimi in the same hand never exceeded 2 ms (stimulating at the wrist). Kimura quotes latency differences between median and ulnar F-responses in the same healthy limb (stimulating at the wrist and recording from thenar and hypothenar muscle) of up to 2.4 ms and in the lower limb for the peroneal and posterior tibial nerves (stimulating at the ankle and recording from intrinsic foot muscles), of up to 4.1 ms (mean + 2 S.D.) (Kimura 1983). In unilateral median or ulnar nerve lesions inter-side F-wave latency differences may be the only abnormality detected on nerve conduction studies. When the fastest conducted F-responses are recorded from abductor pollicis brevis bilaterally the inter-side latency difference is consistently small in health and can provide the basis for a sensitive comparison (Kimura 1983). Lachman and colleagues (1980) found this difference to be less than 2 ms. Right-left latency differences cited by Kimura's laboratory for their healthy control range are as follows: (upper limit cited = mean + 2 S.D.):

median nerve/thenar muscle - 2.3 ms (stimulating at the wrist), ulnar nerve/hypothenar muscle - 2.7 ms (stimulating at the wrist), peroneal nerve/extensor digitorum brevis - 3.5 ms (ankle stimulus), posterior tibial nerve/flexor hallucis - 3.5 ms (ankle stimulus). Comparisons between the right and left limbs of individual subjects have disclosed that in the F-responses recorded from the median nerve/abductor pollicis brevis there is a tendency for the minimal F-wave latency on the right side to be longer (Peioglou-Harmoussi et al 1985(a)). This may represent subclinical median nerve damage in the dominant wrist.

2.1.4. F-ratio

By recording M and F-responses from a stimulus at one site, a ratio of conduction latencies can be obtained and used to compare motor conduction times across the segments distal and proximal to the stimulus. This has been called the F-ratio (Kimura 1978(b)). (F-M-1)/2M (ms) compares the latency for conduction from the stimulus site to the cord, (F-M-1/2) ms, with that for the length of nerve distal to the stimulus, (M) ms (see Figure 2, page 58 for explanation of abbreviations).

Stimulus sites on the ulnar and median nerve near the elbow and for the posterior tibial and peroneal nerves at the knee give ratios near unity (Kimura 1978(b)). One significant advantage of the F-ratio is that estimation of nerve length (always prone to error) is rendered unnecessary and side to side comparisons can be made in individual subjects. A disadvantage, however, is that inter-subject comparison assumes the same proportion between the proximal and distal lengths of the extremities in different individuals. Another assumption made in employing the F-ratio is that motor impulses are conducted across both distal and proximal segments in motor fibres with equivalent conduction characteristics. This can be checked by

totalling the latency of the M and F-responses evoked from an identical single site and comparing this total with that obtained at a more proximal or distal site (Kimura and Butzer 1975). If an increase in latency of the M wave is the same as the concomitant decrease in latency of the earliest F-response when the stimulus is moved, this indicates that the minimal latency F-wave travels centripetally over that nerve segment with the same velocity as the centrifugal impulse evoking the earliest M component.

The stimulation sites which give an F-ratio near 1 are at the popliteal fossa and immediately above the fibular head for the posterior tibial nerve and peroneal nerves respectively. For the median and ulnar nerves, the sites are at the volar crease of the elbow and 3 cm above the medial epicondyle, respectively. Slowing of conduction confined to the proximal segment of the test lower motor neurones results in a ratio which increases. If distal slowing is found when conventional motor nerve conduction velocity is calculated and the F-ratio remains near unity the coexistance of a proximal lesion can be inferred.

2.1.5. F-wave Conduction Velocity

Absolute F-wave latencies can be usefully compared side to side in individual subjects in many instances. If there are circumstances in an individual patient which militate against this F-wave latencies have to be correlated with nerve length (Conrad et al 1975, Lachman et al 1980, Peioglou-Harmoussi et al 1985(a)). As an index of nerve length, either height or limb length have been recommended for use, but Kimura believes that if a measurement of length is to be made it is as well to estimate the length of the segment under test (Kimura 1978(a)). He, and others, have converted F-wave latency data into conduction velocity estimates for the proximal nerve segments (Kimura 1974, Kimura and Butzer 1975, Eisen et al 1977(a),

1977(b), Ongerboer de Visser et al 1982). It can be argued that in doing so accurate measurements are being downgraded by the introduction of inaccurate data needed to make such calculations, e.g. nerve length estimates. The use of an arbitrary figure (1 ms) for the spinal cord "turnaround" time can also be criticised for being inaccurate. No information is available that gives the exact central delay at the anterior horn cell during the genesis of the F-response. The assumption that precisely 1 ms is required as a turnaround time in each motor neurone is unsatisfactory (Young and Shahani 1978). This is particularly so when one considers that the turnaround time could, possibly, be modified by disease processes. The extrapolation from animal data which suggests that the central delay close to 1 ms is unjustified (Gassel et al 1965).

In the upper limb, F-wave conduction velocity has been calculated in the proximal segments of the ulnar and median nerves, and in the lower limbs for the proximal segments of the posterior tibial and peroneal nerves. For the former two, the surface distance from the nerve's stimulus site to the C7 spinous process, via the axilla and mid clavicular point, has been used and for the latter two, the line from the nerve's stimulus site to the T12 spinous process, via the greater trachanter, has been used (Kimura et al 1975, Kimura and Butzer 1975).

Figure 2 illustrates the method for calculating F-wave conduction velocity. The formula used to calculate the F-wave conduction velocity is D x 2 (mm) / F -M -1 (ms), where D is the distance from the stimulus to the appropriate spinous process, (F -M -1 / 2) (ms) is the time required by the fastest conducted F-response to cover the length of nerve, (D), and 1 ms is the delay in the motor neurone pool. F and M (ms) represent F- and M wave latencies obtained with the stimulus at the same site.

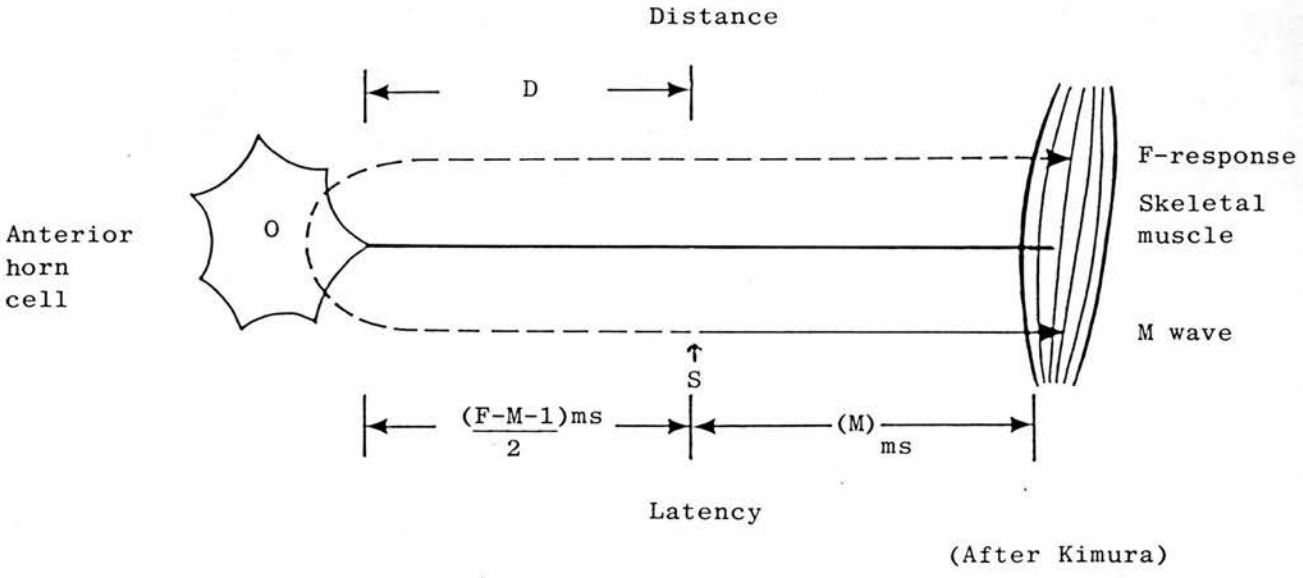


FIGURE 2

METHOD OF CALCULATING F-WAVE CONDUCTION VELOCITY

This schematic representation of an alpha motor neurone and its motor unit territory illustrates how F-wave conduction velocity over the axon's proximal segment (e.g. elbow to spinal cord) is calculated by computing:

2D (mm)/F-M-1(ms) = metres/second

S = stimulus delivered to the proximal nerve trunk (e.g. elbow level)
D = distance from the stimulus site to the surface marker for the ventral horn of the spinal cord
F = F-wave latency
M = M wave latency
$\frac{(F-M-1)}{2}$ ms = latency of conduction over distance D, mm.

Studies of F-wave conduction velocity show that velocities are greater in the proximal segment than in the distal segment, as has been shown for motor nerve conduction velocity, and velocities decrease with age (Kimura 1974, Kimura et al 1975, Eisen et al 1977(a), Ongerboer de Visser et al 1982, Gassel and Trojaborg 1964).

2.1.6. F chronodispersion

The extent of a nerve's F-wave latency range is determined by the motor conduction velocities of its axons, the distance between the test muscle and spinal cord and by central factors which determine which motor neurones can or cannot generate F-responses (Barakan et al 1949, Eccles 1955, Eccles et al 1961, Henneman et al 1965, Trontelj and Trontelj 1973, Schiller and Stålberg 1978, Kimura et al 1984, Shahani et al 1987). In diseased or damaged nerves the conduction of impulses in some motor fibres may be affected more than in others and this can result in a greater range of motor conduction velocities than is found in normal nerves. An extended F-wave latency range in a nerve/muscle can be a sensitive index of motor nerve fibre dysfunction (Panayiotopoulos 1979, Shahani et al 1980(b)).

Minimal and maximal F-wave latencies are used to obtain information on motor conduction in fibres which appear to be the fastest as well as in a range of slightly slower conducting axons (the onset of slowest conducted F-responses cannot be determined using a surface electrode) (Shahani et al 1987). Kimura has shown that slow conducting motor neurones are involved in F-wave production as well as the fastest conducting motor neurones (Kimura et al 1984). Using a collision technique to progressively block fastest conducting motor fibres he was able to prove that F-waves continued to appear in the slower conducting fibres in which collisions did not take place. There is data to correlate the F-wave's minimal latency value with

conduction in the fastest alpha axon (Shahani et al 1987). This experiment illustrated, with a collision technique, that while all but the largest diameter alpha motor axons are refractory for conduction the minimal latency F-response is still conducted. A method of identifying F-wave transmission in the fastest alpha axon(s) involves the recording of a large number of F-wave sweeps and determining the minimal latency value. If, when the stimulus is moved proximally, the increased latency of the earliest M component is the same as the decrease in the minimal F-wave latency (again determined from a large number of F-wave sweeps), it follows that, over that nerve segment, the shortest latency F-wave travels in a centripetal direction at the same speed as the orthodromically transmitted impulse which generates the earliest M component. Trontelj and Trontelj (1973) have provided evidence which shows that completely perfect matching of latencies should not be possible in this technique (see 1.4.1).

F chronodispersion provides a sensitive method for detecting abnormal nerve function in patients with neuropathy and nerve entrapment syndromes, particularly useful when motor nerve conduction velocity remains normal (Panayiotopoulos 1979). In the healthy state, the pattern of F-wave persistence at different latencies within the total F-wave latency range is inconsistent in individual nerves/muscles. For example, either a small or large percentage of the total number of recorded F-waves can have latencies close to the minimum F-wave latency recorded from a large series of F-responses. This has practical importance in the measurement of a muscle's fastest conducted F-response. Small numbers, say 10, as are routinely used, may fail to include the minimal F-wave latency (Shahani et al 1980(b), Lachman et al 1980).

The mechanisms which underly pathological F chronodispersion are likely to be very complex and are not explained simply in terms of slowed conduction peripherally. Panayiotopoulos (1979) attributed excessive chronodispersion to a change in conduction velocity in damaged motor fibres, i.e. suggested that the reason for dispersion was the pathological slowing in the fibres transmitting the recurrent discharge. Alternatively, a different subset of motor neurones may participate in F-wave genesis in the presence of a neuropathic process if the process affects the central "turnaround" time and allows motor neurones which were previously incapable of F-wave genesis to participate in the F-response. It is not known if pathological processes result in delayed F-responses arising from a different subset of motor neurones in the test pool, nor is it known if most delayed F-responses arise from slowed conduction in large motor neurones or from recurrent discharges of smaller motor neurones conducting at their optimal velocities.

Other mechanisms which could be relevant to excess F chronodispersion, such as the derepression of smaller motor neurones will be discussed in Chapter 4 when the effects of peripheral nerve lesions on F-wave persistence will be considered.

In some instances peripheral nerve lesions, such as median nerve entrapments, are not attended by excessive F chronodispersion, while minimal F-wave latency may be grossly delayed (e.g. see 6.9.3). The reasons for this observation are unknown.

F chronodispersion values for healthy ulnar and median nerves recorded from abductor digiti minimi and abductor pollicis brevis, respectively, show no significant inter-side differences, nor has a correlation between F chronodispersion and age or height been identified (Peioglou-Harmoussi 1985(a)). As with inter-side comparisons of minimal latency, inter-side comparisons of F chronodispersion values can be helpful in identifying nerve lesions.

2.2. Studies of F-wave Persistence in Three Different Motor Neurone Pools: An Experiment

2.2.1. Introduction

The practical applications of F-wave analysis in clinical neurophysiology at the present time are based on latency measurements. Other characteristics of the F-response can be quantified and include F-wave persistence, F-complex duration, and F-wave amplitude (Fisher 1978, Fisher et al 1978(a), Eisen and Odusote 1979, Shahani et al 1980(a), Shahani and Sumner 1981, Peioglou-Harmoussi et al 1985(a), Peioglou-Harmoussi et al 1985(b), Petajan 1985). None of these parameters have, so far, been found useful as measurements which can be applied in the EMG lab on a day-to-day basis for the detection of nervous system lesions, particularly lesions of the peripheral nervous system. The changes in F-complex duration and amplitude tend to parallel, either or both, clinical or electromyographic findings and add nothing of much diagnostic worth to the detection of nervous system lesions, including the detection of peripheral nervous system lesions.

The experiments which follow were done to define the recurrent motor discharge patterns of different motor neurone pools. This was done, firstly, to determine if there were significant differences in the F-wave generating behaviour of different motor neurone pools occupying the same and different spinal segmental levels. The second reason for defining the recurrent motor discharge patterns of these different motor neurone pools was to provide control ranges with which to later compare measurements made in patients with diseases of the peripheral nervous system. Theoretically, lesions interrupting the transmission of antidromic motor impulses to the spinal cord might result in a reduction of F-wave persistence as only a reduced fraction of the motor neurone pool could be backfired, i.e. fewer somata would be

invaded antidromically.

There are small amounts of data which suggested that F-wave persistence may differ from one motor neurone pool to another (Fisher 1978). In general, antigravity muscles, e.g. soleus, appear to display higher levels of F-wave persistence than their antagonists. (Fisher used an inadequate number of stimuli, only ten per nerve/muscle, to quantify F-wave persistence in small numbers of muscles). In another study, inter-subject variation in F-wave persistence in the hypothenar muscles has been shown to vary considerably when a large number of stimuli are applied (Peioglou-Harmoussi et al 1985(b)). Schiller and Stålberg's work suggests that an individual motor neurone's liability to issue an F-response when activated antidromically varies in time and that conditions usually prevail to prevent an F-discharge in the majority of cells tested by a single volley (Schiller and Stålberg 1978). F-wave persistence measurements have not been incorporated into electrodiagnostic methods and published data on control subjects is extremely limited; for example, the two papers quoted above include 18 and 21 subjects, respectively.

Initial personal observations suggested that F-wave persistence could be much lower in extensor digitorum brevis than in the intrinsic hand muscles, as recorded by a surface electrode. To see if significant differences in F-wave persistence do exist between different motor neurone pools persistence has been studied in three muscles. The motor neurone pools of two (those of abductor pollicis brevis and abductor digiti minimi) occupy the same spinal segmental level while the third motor neurone pool (that of extensor digitorum brevis) occupies a more caudal position.

As well as studying F-wave persistence, the persistence of identical (same-latency, same-waveform) F-responses has also been incorporated into the analysis of the recurrent discharges from these motor neurone pools.

This was done, firstly, to determine if differences existed between motor neurone pools in the healthy state and, secondly, to provide control values which could be later used to test a hypothesis (see below). The work of Schiller and Stålberg (1978) on F-wave persistence in single motor units showed that, during a train of 200 nerve stimuli (at 1 Hz) the majority of alpha motor neurones innervating abductor digiti minimi failed to generate an F-response and no neurone was seen to produce more than 15. In longer duration experiments (45 minutes stimulating at 1 Hz) periods equivalent to 600 M waves were seen in which no F-responses occurred in single motor neurones. When F-responses appeared they did so in clusters, often following successive stimuli. Magladery and McDougal (1950) noted the variability of latency and form which characterised a sequence of F-responses recorded from the intrinsic hand muscles and this variability relates, it would appear, to varying combinations of single motor units being activated by successive antidromic stimuli (Trontelj and Trontelj 1973, Schiller and Stålberg 1978). The behaviour of motor neurones in the experiments of Schiller and Stålberg may, however, differ from that exhibited when F-waves are recorded routinely in the EMG laboratory using standard techniques, as the stimulus they used to characterise F-response persistence in individual motor neurones was not supramaximal for the M response. It is interesting to note from Schiller and Stålberg's work that there does appear to be a small sub-population of motor neurones supplying abductor digiti minimi which is prone to discharge F-waves more persistently than the majority of the motor neurones in that pool. They found that no motor neurone examined in abductor digiti minimi was incapable of generating an F-response, although very protracted periods of stimulation were necessary to backfire a response in many test neurones. There are, however, differences apparent from muscle to muscle, e.g. in orbicularis oculi it has proved impossible to obtain

F-responses from some motor neurones (Schiller and Stålberg 1978). In a small number of healthy control subjects it been observed, elsewhere, that the number of identical F-waveforms evoked from hypothenar muscle by a train of 200 stimuli is small (Peioglou-Harmoussi et al 1985(b)). The vast majority (97%) of F-response waveforms appeared only once, and of those responses which recurred, approximately 90% were seen no more than five times. This reflects the typical variability of configuration and amplitude of F-waves recorded from individual intrinsic hand muscles. The results of single fibre EMG jitter studies are consistent with the concept that surface recorded F-responses display temporal variability as they represent the summation of motor unit potentials whose participation in the F-response is inconstant (Trontelj and Trontelj 1973).

It might be predicted that disorders of the lower motor neurone (e.g., motor neurone disease) could reduce the size of the motor neurone pool liable to discharge an F-response and result in a reduction in the variability of F-response waveform and latency as well as a reduction in F-wave persistence.

Before testing the hypotheses that lower motor neurone lesions might cause F-wave impersistence and reduced F-waveform variability, the analysis of F-wave persistence and the persistence of identical F-waveforms undertaken in a population of nerves/muscles of healthy volunteers will be presented.

2.2.2. Methods and materials

Methods

The methods for recording F-waves described here apply to the majority of the experiments outlined in this thesis. Rather than reiterate the same methodology which is applied in separate experiments throughout this thesis the reader will be referred back to this description of the methods and equipment used for eliciting and recording F-responses where relevant. If additional or alternative techniques are employed in any of the experiments they will be detailed in the methods sections which preface those experiments (e.g. 6.6, 6.9). Ethical permission and informed patient consent have been referred to for this, and the other experiments, in the introduction to the thesis.

In each experiment in which F-responses were recorded, the method was standardised. The ambient room temperature was maintained above 26°C. Surface skin temperature was measured with a thermistor (Dantec Regulator Unit, Type 15H02) on the volar aspect of the mid forearm or medial aspect of mid calf, whichever was appropriate for each test limb, and the patient's temperature was maintained by means of an electric heater, hot water bottles and blankets so that this reading was at or above 34°C.

F-responses were recorded from the abductor pollicis brevis and abductor digiti minimi muscles stimulating the median and ulnar nerves, respectively, at the wrist (cathode 2 cm proximal to the distal skin crease) and from the extensor digitorum brevis muscle stimulating the deep peroneal nerve at the ankle. The stimulating electrode was a large Medelec bipolar electrode (interelectrode distance 2 cm, contact area 30 mm*sq*) (type LBS 53051). A saddle type of recording electrode with silver/silver chloride disc electrodes, diameter 1 cm, 2.5 cm apart mounted in a perspex holder was

used in all the experiments save 2 (6.6 and 6.9). The active electrode was located over each muscle's motor point, detected by finding the site on the belly of the muscle at which a twitch could be induced by the weakest electric shock, and the indifferent electrode was placed over the muscle's tendon. The stimulating unit was a Medelec MS8, or Medelec MS6, electromyograph which, through a surface bipolar electrode, delivered supramaximal 100 μsec duration square wave shocks at a voltage set to 20% greater than that needed to produce a maximised M wave at 1 Hz. Once the necessary voltage was defined, the polarity of the stimulating electrode was reversed so that the cathode was sited proximal to the anode and the M wave's amplitude was then rechecked before F-waves were recorded. The anode was placed distal to the cathode when recording F-waves to avoid anodal block of the antidromic impulses.

All experiments were done with the subject supine and relaxed to minimise the effects of ipsisegmental (ipsilateral or contralateral) muscular contraction on motor neurone excitability (Hagbarth 1962, Knezevic et al 1985, Fox and Hitchcock 1985). No objective measure of involuntary motor unit recruitment was made in the test muscle or contralateral ipsisegmental muscles. Each subject was instructed to call a halt if he or she found the test uncomfortable and the stimulus was stopped if motor units appeared outwith the F- and M waves on the oscilloscope until such activity was abolished.

Amplification (band pass 20 Hz - 2 KHz, MS8, band pass 1.6 Hz - 3.2 kHz MS6) and oscilloscope sweep speed were set to optimise the display of F-responses. F-wave sweeps were recorded on moving photographic paper on the Raster setting and from these photographs measurements were subsequently made. Only F-responses with a peak to peak amplitude of >40 μV were included in the analysis. Lower voltage deflections were discarded

for ease of interpretation. The waveform of such small potentials could not be characterised with certainty. F-wave latencies were measured from the stimulus artefact to the beginning of the first deflection (usually negative) from the baseline.

One hundred supramaximal stimuli were applied to each test nerve to yield 100 photographed F-wave sweeps for analysis.

Measurements

In this experiment two measurements were made from each test nerve/muscle: 1) F-wave persistence, 2) the Repeater F-wave count.

F-wave persistence is defined as the number of F-responses >40 μV (peak to peak) per 100 M waves. A Repeater F-wave is an individual F-response, with its unique configuration and latency, which is recorded twice or more from an individual muscle. The waveform and latency of each F-response characterise it. Figure 3 provides two examples to show how F-wave persistence and Repeater F-wave counts are calculated. (It should be noted that in the experiments of the thesis 100 F-wave sweeps are used to make the calculations, unlike the illustrative example). F-wave persistence refers to the frequency at which F-responses appear during a train of supramaximal stimuli. The Repeater F-wave count is the total number of Repeater F-waves obtained from 100 stimuli, i.e. the total number of F-waves sweeps in which a Repeater F-wave appears.

In summary, F-wave persistence and Repeater F-wave counts were determined by delivering 100 stimuli to each test nerve and the recordings were made from abductor digiti minimi, abductor pollicis brevis and extensor digitorum brevis.

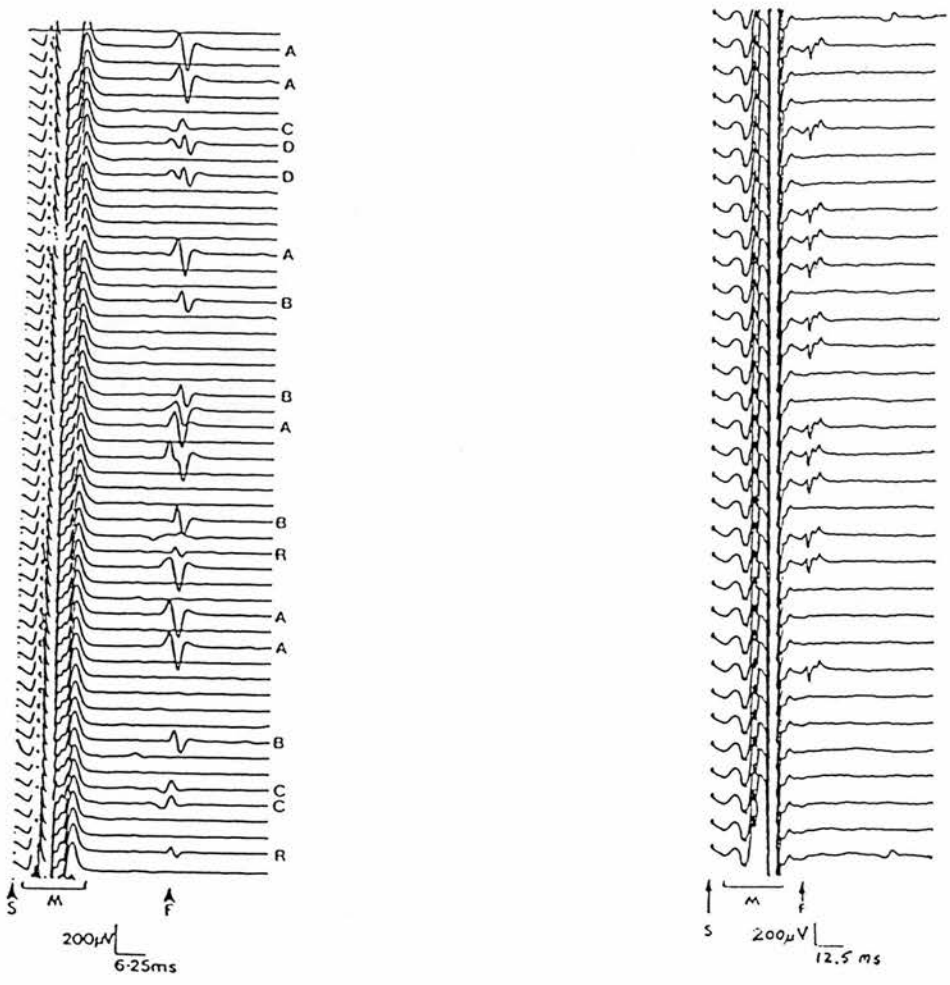


FIGURE 3

IDENTIFICATION OF REPEATER F-WAVES AND CALCULATION OF THE REPEATER F-WAVE COUNT

A: Repeater F-waves recorded from abductor digiti minimi of a patient with cervico-dorsal syringomyelia.
The 53 F-wave sweeps contain 21 F-waves (F-wave persistence value). 5 waveforms appear more than once, types A, B, C, D and R, and are termed Repeater F-waves. A appears 6 times, B 4 times, C 3 times, D twice and R twice. The Repeater F-wave count from these 53 stimuli is 17 (4 less than the F-wave persistence value).

B: Repeater F-waves recorded from abductor pollicis brevis of a patient with Guillain-Barré syndrome.
These F-wave sweeps contain 2 individual Repeater F-waves. The earlier one is highly persistent (appearing in 13 of 32 sweeps), the later Repeater F-wave appears twice (uppermost and lowermost sweeps) and is very delayed.
The Repeater F-wave count from these 32 sweeps is 15, the same as the F-wave persistence value.

(Note: Repeater F-wave counts and F-wave persistence values are derived from 100 stimuli in the experiments of the thesis).

Subjects

To determine F-wave persistence and Repeater F-wave counts in the three test motor neurone pools in health, the following criteria had to be met by apparently "healthy" volunteers before gaining acceptance into the study: there were no symptoms of nervous system dysfunction, no upper or lower motor neurone signs were found on examination, there had been no exposure to neurotoxic drugs (12 subjects took medication for migraine, allergies or asthma, none of which drugs are known to have a neurotoxic effect), there was no history of alcohol abuse, there was no known medical condition present which predisposed to neuropathy (e.g. diabetes mellitus, rheumatoid arthritis) and there was no family history of neuropathy.

Eighty-five deep peroneal nerves from 55 healthy volunteers, 29 female, 26 male, aged 26-65 years (mean 39.9, S.D. 10.9), were studied. One hundred and fifty-three ulnar nerves from 109 healthy subjects, 54 male, 55 female, aged 26-65 years (mean 43, S.D. 9.5) were studied. One hundred and forty-seven median nerves from 99 healthy volunteers, 53 female, 46 male, aged 26-65 years (mean 43, S.D. 9.8) were studied. The groups were comprised of test subjects restricted to 26-65 years and had a comparable age structure. For reasons for this age selection see 2.4. From 1 to 4 nerves were studied in a given individual. The volunteers came mainly from hospital staff and included junior hospital doctors, nurses, laboratory technicians, physiotherapists, speech therapists, staff from the medical photography department, domestic and portering staff. Twelve patients with tension and vascular headache, who had no features suggestive of a potentially relevant peripheral or central nervous system lesion, were included. Thirteen patients being investigated in the EMG laboratory at Dundee Royal Infirmary for lumbosacral root lesions and/or backache volunteered their upper limbs for this experiment.

2.2.3. Results

F-wave persistence

F-wave persistence values for the 3 test groups are listed in Tables 1, 2 and 3. The results are displayed in histographic form in Figure 4.

In the deep peroneal nerve F-wave persistence values ranged from 4 to 100 and were fairly evenly distributed throughout that range. The majority of test nerves/muscles yielded less than 50 F-responses, >40 μV amplitude, per 100 stimuli.

In contrast, values derived from the ulnar nerve were highly skewed. 96% of observations lay above 60 and 83% lay above 80. The range for the ulnar nerves extended from 18 to 100. In only 4 test nerves were persistence values of $\leq$50 found. One hundred F-responses (>40 μV) resulting from 100 stimuli were recorded in approximately 60 of the test ulnar nerves/muscles.

F-wave persistence values from the median nerves were similar in distribution to those from the ulnar nerves, i.e. skewed. 76% of the values were above 80. The range for those nerves went from 25 to 100.

Statistical analysis

As the data was not normally distributed, a non-parametric method, the Mann-Whitney test, was used to determine if there were significant differences in the F-wave persistence values obtained from the three test motor neurone pools. The analysis shows strong evidence of a difference in the F-wave persistence values obtained from the ulnar and peroneal nerve groups ($p<0.0001$), the median and peroneal nerve groups ($p<0.0001$) and the ulnar and median nerve groups ($p=0.0002$).

TABLE 1

ANALYSIS OF F-RESPONSES OF ASYMPTOMATIC VOLUNTEERS AGED 26-65

DEEP PERONEAL NERVE
(n = 85)

Nerve No.	F-wave Persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave Value
1.	46	34	74
2.	68	22	32
3.	73	50	68
4.	82	25	30
5.	33	13	39
6.	29	19	66
7.	28	14	50
8.	88	18	20
9.	66	46	70
10.	85	44	52
11.	44	29	66
12.	64	13	20
13.	90	33	37
14.	72	14	19
15.	90	33	37
16.	90	34	38
17.	40	26	65
18.	5	5	100
19.	40	30	75
20.	20	16	80
21.	37	25	68
22.	36	27	75
23.	44	26	59
24.	45	29	64
25.	50	35	70
26.	7	5	71
27.	33	24	73
28.	78	20	26
29.	8	2	25
30.	11	7	64
31.	4	2	50
32.	9	5	56
33.	49	18	37
34.	58	17	29
35.	14	12	86
36.	77	35	45
37.	68	19	28
38.	43	16	37
39.	56	41	73
40.	67	25	37
41.	87	35	40
42.	78	36	46
43.	34	19	56

Nerve No.	F-wave Persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave Value
44.	10	7	70
45.	47	26	55
46.	100	36	36
47.	65	26	40
48.	48	22	46
49.	20	17	85
50.	43	16	37
51.	38	35	92
52.	74	50	68
53.	58	25	43
54.	77	33	43
55.	12	7	58
56.	63	44	70
57.	54	35	65
58.	53	15	28
59.	5	0	0
60.	47	26	55
61.	19	11	58
62.	30	17	57
63.	23	17	74
64.	19	15	79
65.	31	31	100
66.	90	60	66
67.	26	21	81
68.	42	24	57
69.	45	26	58
70.	14	7	50
71.	71	30	42
72.	95	28	29
73.	21	21	100
74.	4	3	75
75.	49	33	67
76.	53	36	68
77.	84	71	85
78.	90	24	27
79.	52	6	12
80.	25	4	16
81.	22	19	86
82.	19	13	68
83.	12	11	92
84.	32	20	63
85.	81	30	37

TABLE 2

ANALYSIS OF F-RESPONSES OF ASYMPTOMATIC VOLUNTEERS AGED 26-65 YEARS

ULNAR NERVES
(n = 153)

Nerve No.	F-wave persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave value
1	100	5	5
2	90	2	2
3	96	5	5
4	94	10	11
5	90	5	6
6	92	6	7
7	81	5	6
8	80	15	19
9	50	4	8
10	91	10	11
11	78	5	6
12	80	15	19
13	96	8	8
14	78	11	14
15	70	10	14
16	18	0	0
17	30	0	0
18	90	6	7
19	100	4	4
20	92	3	3
21	100	6	6
22	100	5	5
23	98	5	5
24	100	8	8
25	100	0	0
26	100	4	4
27	100	0	0
28	100	6	6
29	99	2	2
30	81	16	20
31	100	8	8
32	100	4	4
33	85	4	5
34	94	8	9
35	100	10	10
36	100	4	4
37	100	4	4
38	100	0	0
39	93	6	6
40	73	23	32
41	46	15	33
42	100	18	18

Nerve No.	F-wave persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave value
43	70	16	23
44	90	18	20
45	100	0	0
46	93	6	6
47	94	12	13
48	100	4	4
49	100	3	3
50	100	0	0
51	100	0	0
52	97	7	7
53	100	5	5
54	100	0	0
55	95	16	17
56	90	6	7
57	92	6	7
58	100	6	6
59	89	0	0
60	100	12	12
61	70	18	26
62	100	12	12
63	100	4	4
64	95	5	5
65	89	2	2
66	96	0	0
67	65	0	0
68	96	9	9
69	53	13	25
70	100	0	0
71	93	4	4
72	100	20	20
73	81	4	5
74	100	12	12
75	100	10	10
76	61	5	8
77	100	12	12
78	100	6	6
79	94	15	16
80	71	4	6
81	100	0	0
82	100	6	6
83	98	25	26
84	60	18	30
85	99	18	18
86	100	0	0
87	96	8	8
88	97	16	16
89	98	32	33
90	88	8	9
91	100	8	8
92	93	17	18
93	96	7	7
94	75	13	17

Nerve No.	F-wave persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave value
95	91	8	9
96	74	6	8
97	100	14	14
98	100	4	4
99	97	7	7
100	90	19	21
101	77	23	30
102	100	0	0
103	96	4	4
104	83	5	6
105	88	5	6
106	100	14	14
107	100	12	12
108	86	12	14
109	100	8	8
110	97	10	10
111	100	0	0
112	92	9	10
113	83	6	7
114	100	5	5
115	96	3	3
116	100	12	12
117	100	11	11
118	90	6	7
119	100	6	6
120	80	13	16
121	74	4	5
122	100	13	13
123	91	16	18
124	100	4	4
125	100	4	4
126	100	11	11
127	98	15	15
128	99	3	3
129	97	16	16
130	100	6	6
131	93	8	9
132	99	5	5
133	81	9	11
134	98	6	6
135	99	2	2
136	100	17	17
137	100	12	12
138	87	0	0
139	92	6	7
140	100	7	7
141	100	6	6
142	100	4	4
143	99	15	15
144	87	6	7

Nerve No.	F-wave persistence value	Repeater F-wave No./100 M waves	%Repeater F-wave value
145	100	6	6
146	80	8	10
147	89	8	9
148	70	15	21
149	70	15	21
150	76	6	8
151	96	5	5
152	100	0	0
153	82	4	5

TABLE 3

ANALYSIS OF F-RESPONSES OF ASYMPTOMATIC VOLUNTEERS AGED 26-65

MEDIAN NERVE
(n = 147)

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave value
1.	89	28	31
2.	100	0	0
3.	76	2	3
4.	100	7	7
5.	60	10	17
6.	25	6	24
7.	75	2	3
8.	90	3	3
9.	34	20	59
10.	89	12	13
11.	100	6	6
12.	78	29	37
13.	90	9	10
14.	90	9	10
15.	72	30	42
16.	88	8	9
17.	88	2	2
18.	80	6	8
19.	80	5	6
20.	80	0	0
21.	75	5	7
22.	75	8	11
23.	100	0	0
24.	85	6	7
25.	96	6	7
26.	92	5	5
27.	100	8	8
28.	100	4	4
29.	100	5	5
30.	100	3	3
31.	95	2	2
32.	90	5	6
33.	100	3	3
34.	73	11	15
35.	100	0	0
36.	87	2	2
37.	90	8	9
38.	95	8	8
39.	87	11	13
40.	92	7	8
41.	83	20	24
42.	100	6	6
43.	65	22	34
44.	81	22	27

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave value
45.	83	14	17
46.	97	13	13
47.	90	8	9
48.	90	10	11
49.	100	6	6
50.	90	6	7
51.	100	0	0
52.	48	2	4
53.	68	14	21
54.	75	23	31
55.	90	5	6
56.	51	21	41
57.	81	8	10
58.	90	14	16
59.	72	16	22
60.	58	35	60
61.	100	0	0
62.	98	13	13
63.	90	10	11
64.	75	21	28
65.	80	0	0
66.	53	18	34
67.	73	15	21
68.	93	6	6
69.	94	13	14
70.	90	10	11
71.	54	26	48
72.	80	26	33
73.	100	6	6
74.	67	3	4
75.	98	16	16
76.	90	24	27
77.	94	4	4
78.	86	4	5
79.	88	19	22
80.	55	2	4
81.	54	13	24
82.	98	12	12
83.	80	9	11
84.	93	6	6
85.	98	15	15
86.	100	8	8
87.	100	20	20
88.	88	5	6
89.	86	17	20
90.	90	4	4
91.	92	6	7
92.	92	17	18
93.	99	6	6
94.	99	25	25
95.	100	11	11
96.	83	16	19
97.	87	14	16

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave value
98.	84	2	2
99.	90	15	17
100.	89	17	19
101.	91	12	13
102.	81	22	27
103.	94	24	26
104.	99	4	4
105.	99	7	7
106.	91	9	10
107.	94	6	6
108.	78	18	23
109.	96	4	4
110.	74	7	9
111.	96	21	22
112.	91	4	4
113.	100	10	10
114.	84	12	14
115.	79	8	10
116.	82	22	27
117.	87	11	13
118.	94	22	23
119.	100	0	0
120.	75	21	28
121.	98	0	0
122.	90	11	12
123.	100	0	0
124.	95	4	4
125.	100	5	5
126.	98	6	6
127.	100	8	8
128.	87	8	9
129.	92	12	13
130.	100	15	15
131.	91	12	13
132.	100	7	7
133.	86	4	5
134.	100	4	4
135.	100	3	3
136.	91	0	0
137.	78	4	5
138.	100	7	7
139.	100	2	2
140.	85	11	13
141.	89	14	16
142.	100	8	8
143.	93	4	4
144.	100	12	12
145.	86	10	12
146.	100	0	0
147.	96	2	2

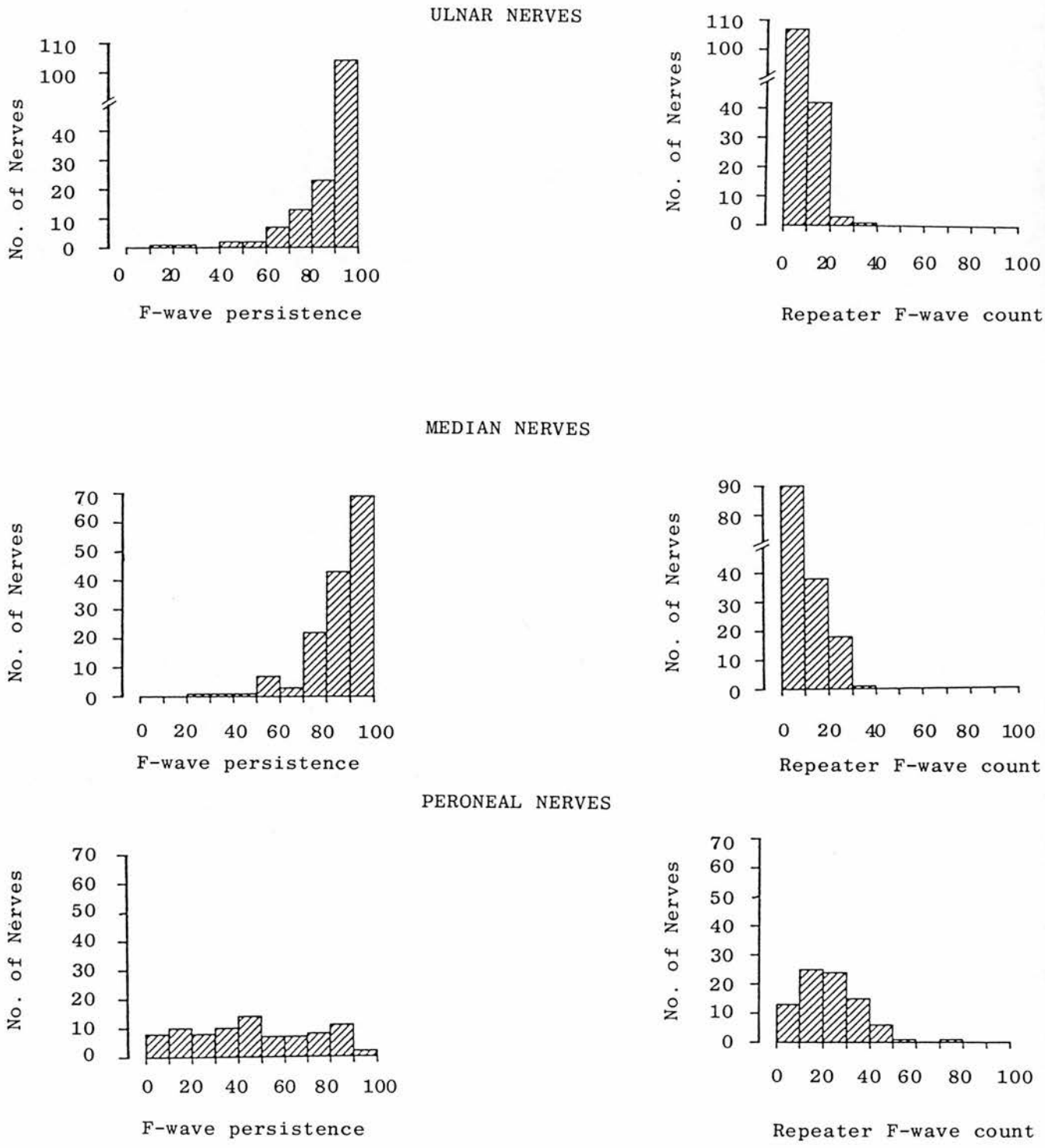


FIGURE 4

F-wave persistence and Repeater F-wave counts from 153 ulnar nerves, 147 median nerves and 85 peroneal nerves from volunteer subjects, aged 26-65 years, without signs or symptoms of nervous system dysfunction.

Repeater F-wave counts

Repeater F-wave values for the 3 test groups are listed in Tables 1, 2 and 3. The results are displayed histographically in Figure 4. Differences in the Repeater F-wave counts for the three groups were, like the persistence values, most obvious between the upper and lower limb motor neurone pools.

In the peroneal nerve group, only one test nerve failed to transmit Repeater F-waves, i.e. each recorded F-response had a unique latency/form in only one test nerve/muscle. Repeater F-wave counts of up to 71 were found although the majority of values (73%) were less than 30.

Figure 5 illustrates a high Repeater F-wave count from a healthy volunteer's extensor digitorum brevis muscle. Multiple individual Repeater F-wave types are seen.

The counts of Repeater F-waves obtained from median and ulnar nerves were more tightly distributed as well as being more skewed.

The range of values in the ulnar nerve group was 0 to 32, only 4 of 153 had values greater than 20 and 70% had a value $\leq$10.

For the median nerves the range was 0 to 35, only one nerve had a value greater than 30. 87% of nerves had counts $\leq$20.

Statistical analysis

The Mann-Whitney test was applied to test for differences in the Repeater F-wave counts between the three groups of test nerves/muscles. There was strong evidence of a significant difference between the ulnar and peroneal nerve groups ($p<0.0001$) and between the median and peroneal nerve groups ($p<0.0001$). Differences in the frequency with which identical F-waveforms were generated in the ulnar and median nerve groups just failed to reach significance at the 5% level ($p=0.057$).

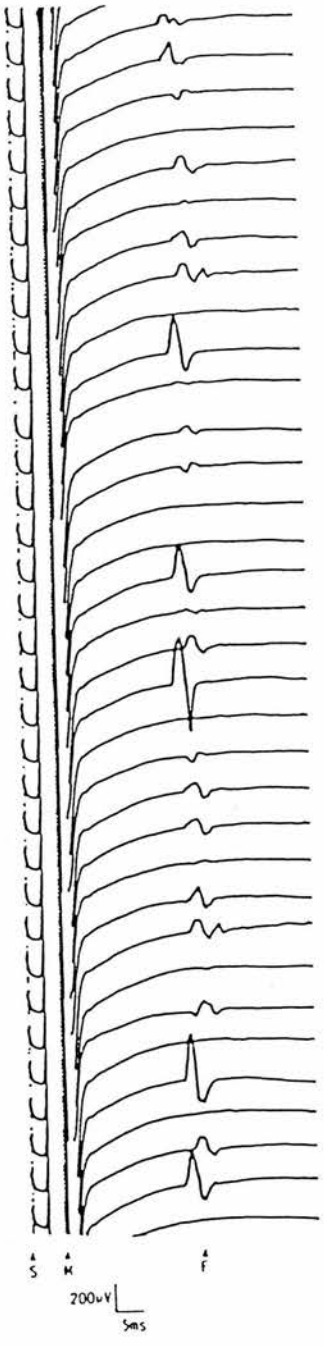


FIGURE 5

F-RESPONSES FROM EXTENSOR DIGITORUM BREVIS

Stimulating the deep peroneal nerve, at the ankle of a healthy 24-year old male, Repeater F-waves occur frequently.

2.2.4. Comments and conclusions

Before commenting on the results obtained, some aspects of the methodology require consideration. Firstly, the identification of Repeater F-waves has not been accomplished in a wholly objective manner. It is easier, in most instances, to identify Repeater F-waves when the F-wave persistence level is low, particularly if Repeater F-waves themselves appear at a high level of persistence.

Secondly, it was sometimes difficult to be certain if 2 F-waves were identical. Some subjectivity, therefore, is attached to the interpretation of the F-wave sweeps recorded.

The differences which have been detected are striking (save for Repeater F-wave counts in the ulnar and median groups) and have not, the author believes, been significantly modified by observer bias.

Thirdly, what impact on the measured F-wave persistence values has the adoption of a minimum 40 μV F-wave amplitude had? The number of F-responses <40 μV has not been computed. However, in the majority of sweeps recorded in which no F-wave >40 μV appeared the trace was flat. The decision to use this criterion was based on practical reasons. The control data obtained from each test muscle has been obtained using the same recording methods (e.g. the same recording electrode) and these methods will be replicated for the determination of values in patients with disorders of the peripheral nervous system. The technique, therefore, is standardised for all subjects. The influence of skin impedance, skin thickness and other local factors which influence the amplitude of the potentials recorded from the underlying muscle, have not been quantified.

The differences between each of the three motor neurone pools in the persistence of F-responses evoked by stimuli delivered at 1 Hz, over a 100 second period, indicates that each pool has its individual liability to

discharge F-waves in response to antidromic activation. The majority of ulnar and median nerves had high F-persistence values (>80), which contrasted with the peroneal nerves, whose motor cells were less active as F-wave generators. There appear to be factors which determine fairly consistent levels of F-wave persistence in the motor neurone pools of abductor pollicis brevis and abductor digiti minimi while there is a much less rigid pattern of backfired activity from the motor neurone pools of the extensor digitorum brevis muscles which have been tested. The mechanisms underlying these differences are not known. The presence of very high F-wave persistence values in some peroneal nerves compared with very low persistence values in others may suggest that it is not the anatomical characteristics of the motor neurone supplying extensor digitorum brevis which bias against F-wave production in some instances. Factors governing F-wave production are poorly understood.

The "size principal" of motor neurone activation does not apply to the F-response (Hennemann et al 1965). The growth of the F-response (in terms of persistence and amplitude) with increasing stimulus intensity differs from the relatively smooth growth of the H-reflex obtained with small graduated stimulus increments (Thorne 1965, Mastaglia and Carroll 1985, Scheippati 1987). The F-wave grows, instead, in an unpredictable manner with increasing stimulus intensity showing great variation in size and persistence from one test muscle to another with equivalent stimuli. When the stimulus is supramaximal the size of the F-response shows a ragged plateau. Sub-maximal stimuli are capable of generating F-responses with the same minimal latency as supramaximal stimuli, but F-wave persistence and amplitude are reduced (Kimura et al 1984). This phenomenon probably represents conduction in low threshold, fast conducting alpha axons of a smaller population of backfired motor neurones. F-waves appear with maximal persistence and amplitude

only when most (or all) of the available motor neurones can be activated antidromically (Thorne 1965). There is evidence to suggest that motor units with largest motor unit potentials are recruited into the F-discharge when stimulus intensities are higher than threshold for earliest recruited motor axons (Feasby and Brown 1974). Yates and Brown (1979) failed to find evidence of a direct relation between a single motor unit's liability to discharge an F-wave and its surface voltage.

There is some evidence, from animal work, which might be used to predict that smaller motor neurones could be at a relative disadvantage in generating F-responses compared with the larger motor neurones (Eccles 1955). Secondly, antidromic activation of the largest and fastest conducting alpha axons results in early orthodromic impulse transmission through those neurones' Renshaw cells which may have significant inhibitory effect on smaller, slower conducting motor neurones' capacity to issue an F-response (Renshaw 1941, Eccles et al 1961).

An additional factor concerning the control of F-discharges relates to the second phase of Renshaw inhibition initiated by the F-discharge itself. (The author is not aware of this having been considered in the literature). Those few motor neurones which discharge an F-response will, consequently, transmit a second impulse through their Renshaw cells following the initial impulse, set up artifically by the antidromic volley, and this could have significant effects on the F-generating capacity of the smaller, slower conducting motor neurones. This secondary wave of Renshaw activity might be expected to have a more significant effect on other cells' ability to issue an F-response in the presence of slowed motor conduction.

F chronodispersion studies do not, however, reveal a distribution of F-latencies in keeping with the fastest fibres always being favoured. Indeed, the distribution can be skewed towards the upper end of the minimum-

maximum F-wave range latency (Panayiotopoulos 1979). Of the mechanisms which prevent motor neurones from being backfired by every or any antidromic stimulus, the depolarisation/repolarisation schedules of individual anterior horn cells are of particular importance (Renshaw 1941, Eccles 1955, Schiller and Stålberg 1978). The antidromic impulse may fail to enter the soma of some motor neurones, as in the cat (Lloyd 1943, Barakan et al 1949). This type of antidromic block is liable to occur at the axon hillock where the membrane surface changes between axon and soma (Eccles 1955). For an antidromic impulse to be propagated out of the soma of the motor neurone, repolarisation of the axon hillock and the proximal segment of the axon must have taken place. The low persistence of F-responses in individual healthy motor neurones suggests that either the invasion of the soma is infrequent and/or the depolarisation/repolarisation schedule blocks the distal passage of the recurrent discharge. It has already been noted that the jitter value of the F-response through individual motor neurones is only marginally greater than that of the M wave in the same neurones (see 1.4.1). Animal experiments have shown that small slower conducting motor neurones are more rapidly depolarised than the larger neurones and in some cells the soma-dendritic spike may appear in advance of axonal repolarisation (Kernell 1966). The capacity of a neurone to issue a recurrent discharge is governed by such membrane characteristics. The effects of maneouvres which modify the membrane potentials of the test anterior horn cells (such as contracting contralateral ipsisegmental muscle) will be discussed in some detail in the section concerning the effects of upper motor neurone lesions on the F-response (see 4.1.12). Briefly, Schiller and Stålberg (1978) have used membrane theory, mainly derived from Eccles work, to explain the effects of voluntary muscle activation on an individual motor neurone's F-wave persistence value. Voluntary contraction of the test

muscle, or the corresponding contralateral muscle, can either raise or lower F-wave persistence in single motor neurones when quantified by single fibre EMG techniques. In some motor neurones which exhibit high persistence levels at rest, voluntary contraction can induce a fall of F-wave persistence, possibly by advancing the soma-dendritic spike so that it could no longer match the later repolarisation of the axon hillock.

In considering the fraction of the motor neurone pool which issues the F-response, the differences in persistence and Repeater F-wave counts identified in the three motor neurone pools of this experiment are of interest. Peroneal nerves often transmitted infrequent F-responses (e.g. 5 per 100 stimuli), each of which might be a Repeater F-wave i.e. although the motor neurone pool issued a backfired response infrequently, a small but apparently constant fraction of the motor neurone pool acted as the F-wave generator. In the ulnar and median nerves, the highest Repeater F-wave counts were made up by up to 14 (and usually 5-10) individual types of Repeater F-waves, each appearing at low persistence levels, not by one or two individual types of Repeater F-wave appearing persistently, as could be seen in the peroneal nerve. These findings suggest that only a small fraction of the motor neurone pool of extensor digitorum brevis generates recurrent discharges in some healthy subjects in a 100 second period of antidromic stimulation and that those motor neurones which act as F-generators can do so in consort with other motor neurones in fixed combinations at high levels of persistence. Persistent, composite, recurrent motor neurone discharges are much less frequent in median and ulnar nerves (to the muscles tested), in which more variable groupings of motor neurones appear to constitute the F-responses. Schiller and Stålberg's work suggested that, in the hypothenar muscles, infrequent activity in a large part of the motor neurone pool was responsible for the variability of the F-waveforms (although data derives

from stimuli not supramaximal for the M wave). The relationship between the patterns of recurrent discharges to the size of the test motor neurone pool is, in this experiment, uncertain.

The most notable findings from this work are that fixed combinations of motor unit recurrent discharges are infrequent in the hypothenar and thenar muscles while they can be persistent in extensor digitorum brevis. Secondly, F-wave persistence differs in the 3 motor neurone pools tested, the differences being most striking between the lower and upper limb muscles tested. Also, differences in F-wave production in ipsisegmental motor neurones, supplying intrinsic hand muscles, have been found.

It is important that the differences in the F-wave generating patterns which obtain in different motor neurone pools are appreciated before the effects of pathological disorders on these discharge patterns are assessed.

2.3 The %Repeater F-wave Value: A New Measurement for Quantifying F-wave Discharge Patterns. Values from 3 Motor Neurone Pools

2.3.1. Introduction

Preliminary observations on F-wave persistence and the persistence of identical F-waveforms (Repeater F-waves) in patients with disorders of the lower motor neurone (e.g. motor neurone disease) indicated that F-wave persistence could be very low and that, associated with this impersistence of the F-response, F-waveforms could lack the variability typical of the F-response recorded from the healthy thenar and hypothenar muscles. The F-responses could lack variability to an extent wherein responses were comprised largely or even wholly of Repeater F-waves (either one or multiple individual types of Repeater F-waves). Figure 6 illustrates this combination of a low level of F-wave persistence and a high Repeater F-wave count. The F-wave sweeps are from abductor pollicis brevis of a patient with Guillain-Barré syndrome. The persistence level is within the range seen in health, (though on the low side), but the lack of variability in F-waveform is not. The illustration shows 39 F-wave sweeps and 7 F-waves, of which 6 are Repeater F-waves (made up by one individual Repeater F-wave type). The whole set of 100 sweeps has not been illustrated, but in total, from 100 sweeps 26 F-responses were recorded, of which 15 were Repeater F-waves. The absolute Repeater F-wave count (15 per 100) is within the normal value obtained from the muscle in the healthy state (see 2.2.3). Quantification of this observed disturbance in F-generator activity cannot be done by measuring the persistence value alone or by counting the Repeater F-waves. To obtain a measurement which could reflect both F-wave impersistence and reduced variability in the configuration of the F-response (both predicted to result from a contraction in size of the motor neurone pool capable of

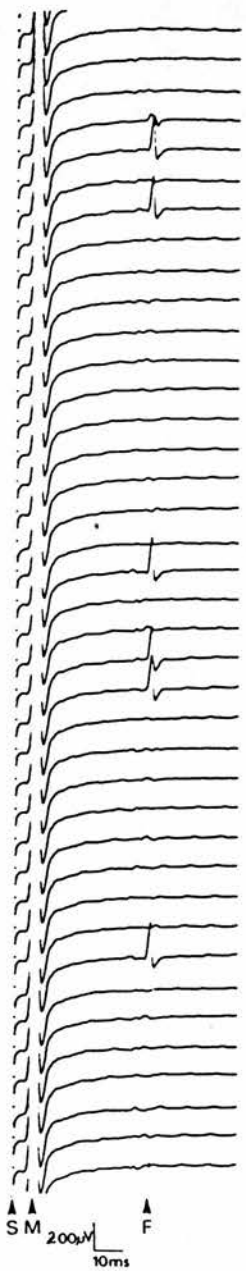


FIGURE 6

Impersistent F-responses comprised of Repeater F-waves. Recorded from abductor pollicis brevis of a patient with acute Guillain-Barré syndrome.

F-wave persistence value = 7 from the 39 sweeps displayed. The Repeater F-wave count = 6.

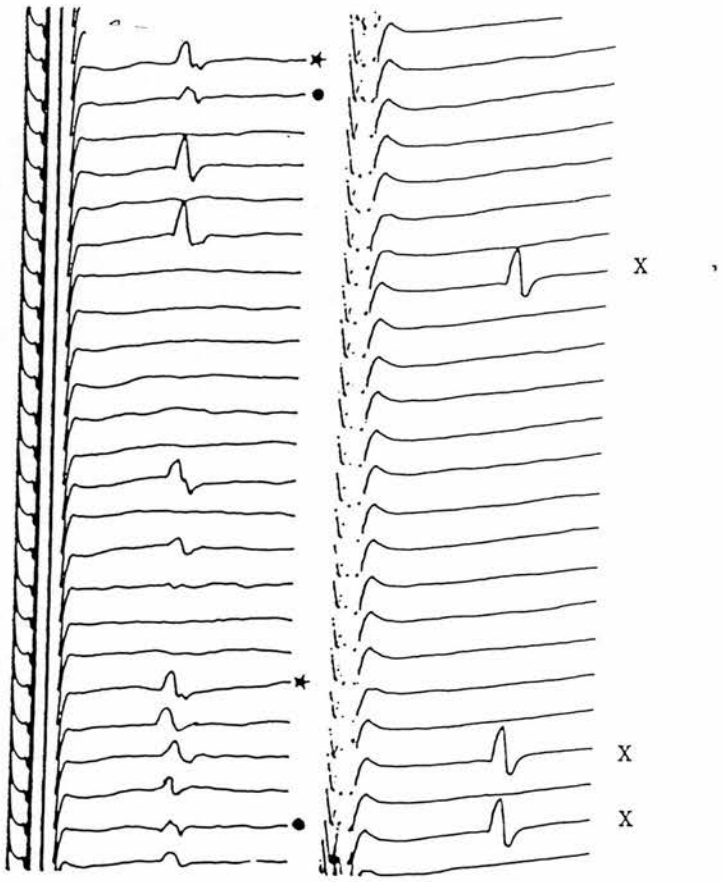
generating F-responses), a new measurement was devised: the %Repeater F-wave value (it will be seen later that unexpected changes in the pattern of F-wave production induced by disorders of the peripheral nervous system also occur - but these, too, can be identified using the %Repeater F-wave value).

The %Repeater F-wave value for a nerve/muscle is the number of Repeater F-waves (>40 μV) expressed as a percentage of the total number of recorded F-waves (>40 μV) derived from 100 supramaximal stimuli, i.e.,

$$\frac{\text{Total number of same-latency, same-waveform individual F-responses occurring twice or more (Repeater F-wave count)}}{\text{Total number of F-waves}} \times \frac{100}{1}$$

This measurement is designed to provide a crude index of the size of the subfraction of the motor neurone pool which is active as an F-wave generator across the full spectrum of F-wave persistence values. Figure 7 provides 2 examples (A, B) of the method of calculating the %Repeater F-wave value. In A and B the total number of Repeater F-waves obtained from 24 stimuli is similar (4 in A and 3 in B). The impersistence of the F-response in B results, however, in a %Repeater F-wave value of 100%. In A, due to the presence of a higher level of persistence, the computed %Repeater F-wave value is much lower at 33%.

Quantification of F-response patterns of 3 different motor neurone pools has been done primarily to provide control values with which to compare values obtained from damaged nerves and to illustrate the differences in F-wave persistence and Repeater F-wave counts already detected.



	[A]	[B]
No. of M waves	24	24
F-wave persistence value	12	3
Repeater F-wave count	4	3
%Repeater F-wave value	4/12 = 33%	3/3 = 100%

FIGURE 7

CALCULATION OF THE %REPEATER F-WAVE VALUE

Repeater F-waves are totalled and expressed as a percentage of the total number of obtained F-responses. In (A) 2 individual Repeater F-waves are present (each twice *, •) and give a Repeater F-wave count of 4. In [B] 1 individual Repeater F-wave is seen in 3 sweeps and, as it consititutes all the F-responses, gives a %Repeater F-wave value of 100%.

2.3.2. Methods and materials

Using the F-wave persistence values and Repeater F-wave counts from the nerves/muscles of the 3 test groups described in 2.2.2., (i.e. 153 ulnar nerves/abductor digiti minimi muscles, 147 median nerves/abductor pollicis brevis muscles, and 85 deep peroneal nerves/extensor digitorum brevis muscles of healthy volunteers aged 26-65 years), %Repeater F-wave values were calculated and comparisons between the ranges of values obtained for the three test motor neurone pools were made. The methods of eliciting and recording the F-waves are described in 2.2.2.

2.3.3. Results

The results can be found in Tables 1, 2 and 3 (pages 72 - 80) and are illustrated histographically in Figure 8. The F-persistence values and Repeater F-wave counts are displayed with the %Repeater F-wave values derived from them for ease of interpretation. The %Repeater F-wave values calculated for the test groups of nerves/muscles gives similar ranges and distributions for the ulnar and median nerves. The highest values observed in the ulnar and median nerve groups were 33% and 60% respectively. Eleven of the 147 test median nerves had %Repeater F-wave values >30% and 12 of the 153 test ulnar nerves had values >20%. The observations were less widely scattered in the ulnar group. In the peroneal nerve group %Repeater F-wave values ranged between 0 and 100% and did not have the skewed distribution of the the two other groups.

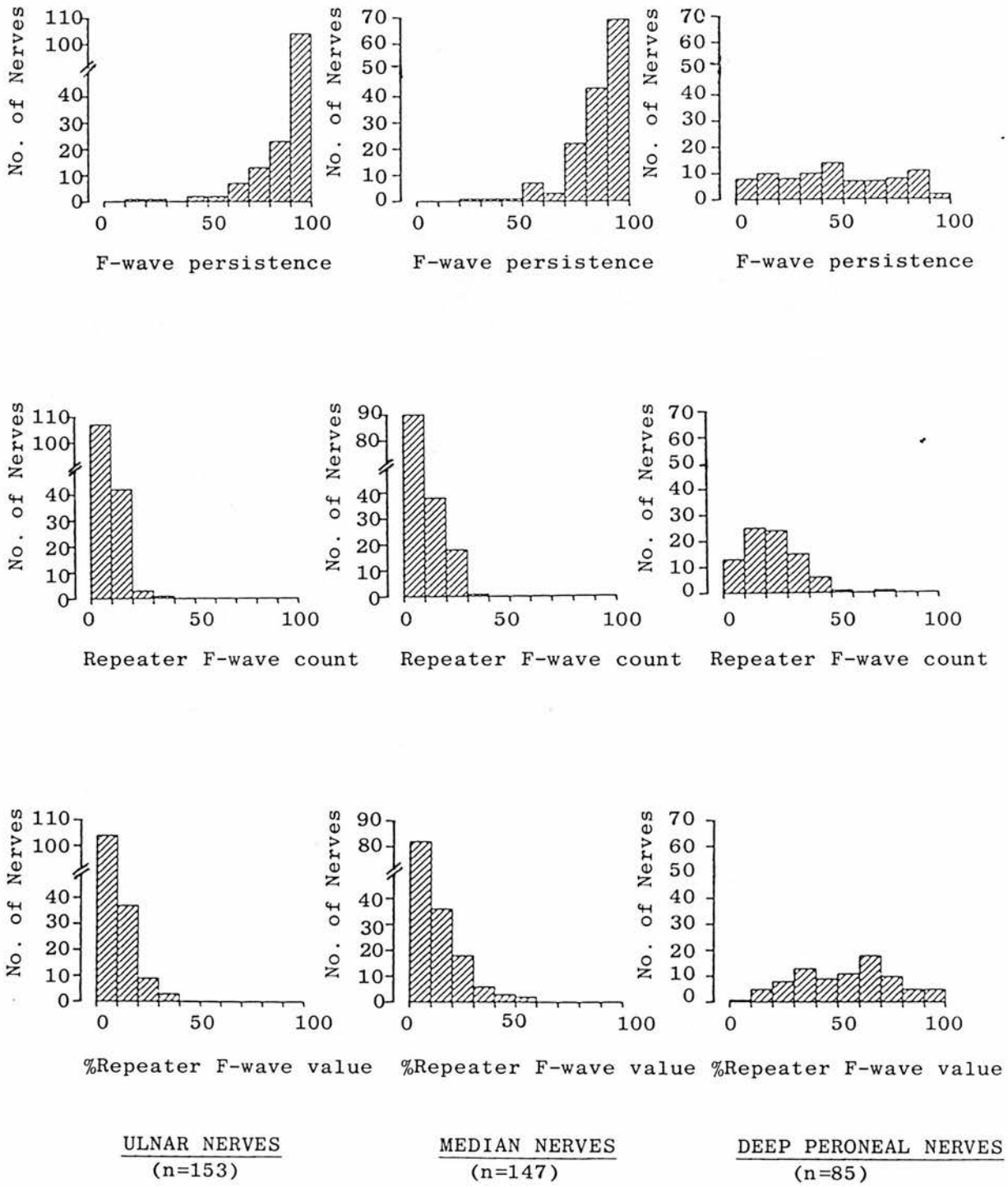


FIGURE 8

%Repeater F-wave values, F-wave persistence values and Repeater F-wave counts of groups of ulnar nerves/abductor digiti muscles, median nerves/abductor pollicis brevis muscles and deep peroneal nerves/extensor digitorum brevis muscles of healthy volunteer subjects aged 26-65 years.

Statistical Analysis

Using the Mann-Whitney test, significant differences in the %Repeater F-wave values of the ulnar nerve and peroneal nerve groups ($p<0.0001$) and the median nerve and peroneal nerve groups ($p<0.0001$) were detected. Differences between the ipsisegmental upper limb groups of test nerves reached significance at the 2% level ($p=0.02$).

2.3.4. Comments and conclusions

The %Repeater F-wave values in the three groups reflect differences in the patterns of response to antidromic activation already detected by F-wave persistence and Repeater F-wave counts. It is important to appreciate these differences before measurements can be applied to patients with peripheral nerve lesions. The peroneal nerve/extensor digitorum brevis can display both impersistent and persistent F-responses, either of which pattern can be made up of a high or low Repeater F-wave count. This is reflected in the spread of %Repeater F-wave values from 0 - 100%. For this reason quantification of F discharges to detect peripheral nerve lesions would not appear to be applicable to that nerve/muscle.

The amplitude ratio of the F-wave to the M wave has been used to suggest that the recurrent discharge occupies approximately 1% of the total number of motor neurones activated antidromically (Eisen and Odusote 1979, Kimura et al 1984). Such calculations can, at best, be only rough approximations for a variety of reasons. Surface electrode recordings may fail to detect the electrical activity of single motor units (Yemm 1977) or parts of motor units depending on a variety of factors which include the size of the motor unit, the skin resistance and the spatial orientation of the motor unit in relation to the recording electrode. The temporal, as well as the spatial, relationship of the potentials arising from multiple synchronously

activated motor units is also a very important determinant of the voltages and configuration of the F-response recorded by a surface electrode. Calculating the number of motor units participating in the F-response using the F- and M wave amplitudes also assumes that each motor unit is of identical size and has an identical spatial relationship with the recording electrode. Motor units, of course, vary in size (Feasby and Brown 1974). At the present time the composition of individual surface recorded F-responses, in terms of the sizes of the contributory motor units, is unknown. Clearly only a small percentage of the motor neurone pool responds to a single antidromic volley at any one time. This small amplitude response could represent a large fraction of the motor neurone pool responding infrequently, a small varying fraction of the pool responding frequently, or a combination of the two. The liability of groups of motor neurones in extensor digitorum brevis to be backfired synchronously (in fixed combinations) appears to be much greater in comparison with the intrinsic hand muscles. A different liability to generate high %Repeater F-wave values has also been identified in the hypothenar and thenar motor neurone pools. The persistence rates of recurrent activity in subfractions of the motor neurone pools is intriguing and the effects which lesions of the peripheral nervous system and lesions of the ipsisegmental spinal cord have on these grouped recurrent motor neurone responses will be detailed in Chapters 4, 5, and 6.

2.4. The Effect of Age on F-wave Persistence and the %Repeater F-wave Value

2.4.1. Introduction

Electrophysiological studies show that, with increasing age, M wave amplitudes tend to decline, particularly after the age of 60, and motor unit threshold firing rates fall (Brown 1972, Campbell et al 1973, McDonagh et al 1987). Age is a determinant of F-wave latency, though, in adulthood, it is less significant than height. Increasing age can be correlated with an increase in the F-wave amplitude calculated as a percentage of the M amplitude (Peioglou-Harmoussi et al 1985(a)). It is not known if this is related to an increase in size of motor units with the advance of age or whether the test motor neurone pool responds differently to an antidromic volley in advanced years. To determine if age should be accounted for, when the F-wave generating behaviour of a motor neurone pool is quantified, an analysis of the relationship of age to F-wave persistence and the %Repeater F-wave value has been undertaken.

The F-wave generating behaviour of the motor neurone pools of abductor pollicis brevis and abductor digiti minimi have been studied in healthy volunteers, of different ages, to see if there is a detectable age-related change. To quantify their F-wave production, measurements of F-wave persistence and %Repeater F-wave values have been made. These two measurements will be used in later experiments (4.3, 5.2, 5.3, 5.4, 6.5, 6.6 and 6.7) to assess the impact of peripheral nervous system lesions on the liability of the motor neurones of abductor pollicis brevis and abductor digiti minimi to discharge F-waves in response to trains of antidromic stimuli.

2.4.2. Methods and Materials

The techniques for eliciting and recording F-waves and the equipment used are described in 2.2.2. The same stimulating and recording paradigm applies in these studies. The methods of calculating F-wave persistence and the %Repeater F-wave value are the same as will be used in experiments on pathological material and these have been described and illustrated earlier: see 2.2.2. and 2.3.1. The entry criteria applied to the asymptomatic volunteers necessary for acceptance into the study are listed in full in 2.2.2. In brief, no identifiable predisposition to peripheral neuropathy or central nervous system dysfunction was identified (e.g. alcohol abuse, the ingestion of neurotoxic drugs or family history of a genetically determined neuropathy). As well as having no symptoms of a central nervous system lesion, each subject had no signs of either a peripheral, or central, nervous system lesion. The sources of volunteers are listed in 2.2.2. Thirty subjects took medication, none of which was associated with neurotoxicity. The "incidental" illnesses of the volunteer subjects included migraine, tension headache, hay fever, asthma, backache and lumbosacral radiculopathy.

Two hundred and forty-seven median nerves and from 156 volunteers, 67 males and 89 females, aged 13-80 years, and 242 ulnar nerves from 163 volunteers, 71 males and 92 females, aged 17 to 82 years were studied. As different motor neurone pools may display different F-wave generating behaviour (see 2.2 and 2.3) the analysis was done on ulnar nerves and median nerves separately.

The age groups assigned for the purposes of the analysis were selected somewhat arbitrarily. It seemed reasonable to consider 10 year epochs. However, it proved logistically difficult to obtain suitable numbers of older and younger volunteers who were healthy, and for this reason nerves from

subjects under the age of 26 were taken as a single group (the youngest subject was 13) and nerves from subjects aged over 65 years were assigned to a single group. The age composition of the material studies is tabulated on pages 101 to 114. The group of oldest subjects ranged from 66 - 80 years for the median nerves and 66 - 82 years for the ulnar nerves. There were at least 30 test nerve/muscles in each age group for both median and ulnar nerves.

2.4.3. Results

F-wave persistence values and %Repeater F-wave values from each individual nerve/muscle examined are listed in Tables 4 and 5. The values are grouped according to age in Tables 6, 7, 8 and 9. For each age group, the mean and standard deviations for the F-wave persistence measurement and the %Repeater F-wave value are listed in Tables 10 and 11. Figures 9 and 10 (see pages 117 to 119) provide a visual display of the results in the form of Box and Whisker plots.

Statistical Analysis

The data from the ulnar and median populations were analysed separately. The analysis was performed in two steps. Initially, a one-way analysis of variance was done to determine if there were significant differences between the age groups. If a significant difference was found the analysis of variance was complemented with the Tukey multiple range comparison procedure, to establish where the differences lay.

The results of the statistical analysis, including the one-way analysis of variance and the Tukey multiple range analysis tests are contained in Tables 12-15 (see pages 120 - 123).

TABLE 4

ANALYSIS OF F-RESPONSES OF ASYMPTOMATIC VOLUNTEERS

MEDIAN NERVES
(n = 247)

Nerve No.	F-wave Persistence Value	Repeater F-Wave No./100 M waves	%Repeater F-wave Value	Age
1.	89	28	31	50
2.	100	0	0	36
3.	76	2	3	28
4.	60	22	37	22
5.	83	6	7	"
6.	65	21	32	22
7.	100	7	7	36
8.	70	10	14	70
9.	77	22	29	"
10.	70	34	49	19
11.	82	8	10	"
12.	60	10	17	50
13.	25	6	24	"
14.	75	2	3	28
15.	90	3	3	61
16.	80	10	13	74
17.	85	10	12	73
18.	100	8	8	"
19.	50	22	44	21
20.	34	20	59	52
21.	89	12	13	40
22.	100	6	6	40
23.	78	29	37	25
24.	100	15	15	68
25.	73	9	12	70
26.	87	2	2	"
27.	87	16	18	20
28.	86	11	13	"
29.	90	9	10	64
30.	90	9	10	59
31.	72	30	42	33
32.	88	8	9	44
33.	88	2	2	"
34.	80	6	8	31
35.	80	5	6	48
36.	80	0	0	"
37.	75	5	7	58
38.	75	8	11	"
39.	60	8	13	21
40.	75	7	9	26
41.	70	0	0	"
42.	80	4	5	21
43.	76	8	11	"

Nerve No.	F-wave Persistence Value	Repeater F-Wave No./100 M waves	%Repeater F-wave Value	Age
44.	69	10	14	20
45.	81	15	19	"
46.	85	5	6	25
47.	80	6	8	"
48.	61	18	30	24
49.	70	6	9	"
50.	58	13	22	22
51.	85	7	8	"
52.	100	0	0	29
53.	85	6	7	"
54.	66	29	44	73
55.	92	4	4	"
56.	67	4	6	21
57.	83	3	4	"
58.	96	7	7	51
59.	92	5	5	"
60.	90	8	9	73
61.	91	7	8	"
62.	100	8	8	63
63.	95	16	17	"
64.	100	4	4	39
65.	100	5	5	46
66.	100	3	3	"
67.	95	2	2	39
68.	90	5	6	"
69.	67	16	24	69
70.	54	8	15	72
71.	90	8	9	"
72.	100	3	3	40
73.	42	10	24	20
74.	15	0	0	20
75.	73	11	15	48
76.	100	0	0	36
77.	46	16	35	23
78.	40	14	35	"
79.	87	2	2	29
80.	90	10	11	17
81.	90	8	9	37
82.	85	15	18	13
83.	90	9	10	"
84.	95	8	8	63
85.	87	11	13	41
86.	92	7	8	"
87.	73	21	29	22
88.	75	14	19	"
89.	100	6	6	15
90.	82	16	20	20
91.	74	28	38	18
92.	76	38	50	"
93.	97	10	10	24

Nerve No.	F-wave Persistence Value	Repeater F-Wave No./100 M waves	%Repeater F-wave Value	Age
94.	94	36	38	"
95.	83	20	24	36
96.	100	6	6	"
97.	65	22	34	41
98.	81	22	27	"
99.	83	14	17	26
100.	97	13	13	"
101.	87	8	9	19
102.	90	8	9	42
103.	90	10	11	"
104.	77	16	21	68
105.	74	31	42	"
106.	100	6	6	37
107.	90	6	7	"
108.	100	0	0	32
109.	48	2	4	42
110.	68	14	21	56
111.	75	23	31	"
112.	90	5	6	31
113.	51	21	41	26
114.	81	8	10	"
115.	76	18	24	24
116.	97	8	8	"
117.	90	14	16	36
118.	72	16	22	"
119.	58	35	60	38
120.	100	0	0	"
121.	98	13	13	62
122.	90	10	11	43
123.	75	21	28	"
124.	80	0	0	29
125.	53	18	34	32
126.	73	15	21	"
127.	93	6	6	26
128.	94	13	14	43
129.	90	10	11	"
130.	54	26	48	45
131.	80	26	33	"
132.	100	6	6	26
133.	67	3	4	55
134.	62	16	26	24
135.	76	5	7	"
136.	90	18	20	23
137.	71	20	28	"
138.	99	11	11	24
139.	98	10	10	"
140.	30	18	60	23
141.	79	25	32	"
142.	60	7	12	25
143.	75	12	16	"
144.	84	4	5	21
145.	100	15	15	"

Nerve No.	F-wave Persistence Value	Repeater F-Wave No./100 M waves	%Repeater F-wave Value	Age
146.	98	16	16	39
147.	90	24	27	42
148.	94	4	4	57
149.	86	4	5	28
150.	88	19	22	53
151.	77	7	9	66
152.	36	8	22	"
153.	55	2	4	48
154.	72	12	17	69
155.	70	12	17	69
156.	82	9	11	74
157.	54	13	24	32
158.	98	12	12	"
159.	100	16	16	21
160.	93	20	22	"
161.	80	9	11	46
162.	83	13	16	23
163.	93	6	6	47
164.	98	15	15	"
165.	100	8	8	57
166.	100	20	20	"
167.	88	5	6	47
168.	86	17	20	"
169.	90	4	4	39
170.	92	6	7	"
171.	87	17	18	57
172.	93	22	24	18
173.	99	6	6	30
174.	99	25	25	"
175.	100	11	11	48
176.	83	16	19	32
177.	87	14	16	30
178.	84	2	2	"
179.	90	15	17	54
180.	89	17	19	"
181.	99	9	9	73
182.	100	10	10	"
183.	91	12	13	52
184.	81	22	27	33
185.	94	24	26	"
186.	99	4	4	52
187.	99	7	7	"
188.	98	25	26	72
189.	100	20	20	"
190.	95	19	20	26
191.	88	12	14	"
192.	91	9	10	42
193.	94	6	6	"
194.	78	18	23	31
195.	96	4	4	"
196.	100	5	5	63
197.	98	4	4	19

Nerve No.	F-wave Persistence Value	Repeater F-Wave No./100 M waves	%Repeater F-wave Value	Age
198.	90	6	7	"
199.	74	7	9	52
200.	96	21	22	31
201.	100	21	21	21
202.	91	4	4	34
203.	100	10	10	52
204.	84	12	14	33
205.	79	8	10	26
206.	82	22	27	"
207.	87	11	13	29
208.	94	22	23	30
209.	100	0	0	"
210.	75	21	28	52
211.	98	0	0	28
212.	90	11	12	"
213.	53	7	13	67
214.	81	6	7	"
215.	90	4	4	68
216.	83	8	10	"
217.	100	0	0	38
218.	95	4	4	"
219.	100	5	5	57
220.	98	6	6	"
221.	100	8	8	36
222.	87	8	9	59
223.	92	12	13	"
224.	100	15	15	63
225.	91	12	13	"
226.	100	7	7	56
227.	86	4	5	"
228.	81	12	15	65
229.	73	14	19	"
230.	91	5	5	66
231.	88	12	14	"
232.	100	4	4	47
233.	100	3	3	"
234.	91	0	0	52
235.	78	4	5	"
236.	100	7	7	58
237.	100	2	2	"
238.	85	11	13	60
239.	89	14	16	"
240.	100	8	8	49
241.	93	4	4	"
242.	76	8	11	80
243.	71	15	21	"
244.	98	3	3	65
245.	96	8	8	"
246.	100	12	12	58
247.	86	10	12	"

TABLE 5

ANALYSIS OF F-RESPONSES OF ASYMPTOMATIC VOLUNTEERS

ULNAR NERVE
(n = 242)

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave Value	Age
1.	80	4	5	67
2.	80	8	10	"
3.	90	0	0	82
4.	95	2	2	78
5.	100	5	5	58
6.	90	2	2	60
7.	96	5	5	58
8.	94	10	11	"
9.	90	5	6	54
10.	92	6	7	"
11.	81	5	6	50
12.	80	15	19	"
13.	50	4	8	34
14.	100	20	20	74
15.	90	10	11	"
16.	91	10	11	30
17.	78	5	6	"
18.	100	3	3	68
19.	80	15	19	40
20.	84	8	10	25
21.	96	8	8	34
22.	78	11	14	"
23.	99	4	4	70
24.	100	17	17	20
25.	70	10	14	59
26.	84	12	14	25
27.	100	28	28	72
28.	99	5	5	"
29.	18	0	0	44
30.	30	0	0	"
31.	90	8	9	22
32.	90	6	7	32
33.	100	4	4	27
34.	95	5	5	73
35.	96	4	4	"
36.	92	3	3	63
37.	100	12	12	73
38.	100	15	15	"
39.	100	6	6	44
40.	91	3	3	23
41.	87	3	3	"
42.	100	6	6	69
43.	100	5	5	54
44.	98	5	5	"

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave Value	Age
45.	100	8	8	26
46.	100	0	0	"
47.	100	4	4	36
48.	100	0	0	"
49.	100	6	6	38
50.	99	2	2	"
51.	81	16	20	61
52.	100	8	8	"
53.	100	4	4	29
54.	85	4	5	"
55.	95	5	5	21
56.	90	6	7	"
57.	94	8	9	63
58.	100	10	10	41
59.	100	4	4	42
60.	100	4	4	"
61.	100	0	0	37
62.	93	6	6	42
63.	73	23	32	49
64.	46	15	33	"
65.	95	5	5	77
66.	94	5	5	"
67.	100	18	18	37
68.	70	16	23	27
69.	90	18	20	"
70.	100	0	0	41
71.	93	6	6	"
72.	94	12	13	33
73.	100	4	4	38
74.	100	3	3	"
75.	100	0	0	32
76.	100	0	0	"
77.	97	7	7	44
78.	100	5	5	"
79.	100	0	0	42
80.	95	16	17	56
81.	90	6	7	43
82.	92	6	7	"
83.	100	6	6	38
84.	89	0	0	62
85.	100	12	12	43
86.	70	18	26	"
87.	100	12	12	58
88.	100	4	4	"
89.	95	5	5	29
90.	89	2	2	52
91.	96	0	0	"
92.	90	14	16	21
93.	99	4	4	24
94.	92	6	7	"
95.	100	17	17	67
96.	64	21	33	"

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave Value	Age
97.	75	8	11	25
98.	61	13	21	"
99.	88	8	9	21
100.	100	5	5	"
101.	65	0	0	53
102.	96	9	9	39
103.	53	13	25	42
104.	100	0	0	62
105.	93	4	4	"
106.	100	20	20	47
107.	81	4	5	26
108.	100	12	12	60
109.	100	10	10	"
110.	61	5	8	26
111.	100	12	12	28
112.	100	6	6	"
113.	94	15	16	51
114.	71	4	6	53
115.	100	0	0	65
116.	100	6	6	48
117.	98	25	26	40
118.	60	18	30	62
119.	99	18	18	"
120.	30	3	10	22
121.	100	0	0	37
122.	96	8	8	56
123.	97	16	16	43
124.	98	32	33	41
125.	88	8	9	36
126.	100	8	8	"
127.	93	17	18	46
128.	96	7	7	46
129.	75	13	17	43
130.	91	8	9	57
131.	74	6	8	47
132.	100	14	14	55
133.	100	4	4	47
134.	97	7	7	39
135.	90	19	21	57
136.	96	12	12	"
137.	77	23	30	60
138.	100	0	0	53
139.	96	4	4	"
140.	83	5	6	27
141.	88	5	6	"
142.	100	14	14	48
143.	100	12	12	"
144.	86	12	14	62
145.	98	14	14	18
146.	100	8	8	38
147.	97	10	10	52
148.	100	0	0	48

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave Value	Age
149.	92	9	10	32
150.	83	6	7	30
151.	100	5	5	54
152.	96	3	3	"
153.	99	4	4	73
154.	100	0	0	"
155.	100	12	12	52
156.	100	11	11	"
157.	90	6	7	47
158.	100	6	6	"
159.	80	13	16	33
160.	74	4	5	"
161.	100	13	13	52
162.	91	16	18	"
163.	100	4	4	51
164.	100	4	4	"
165.	100	16	16	24
166.	100	10	10	24
167.	98	12	12	17
168.	96	11	11	"
169.	100	11	11	42
170.	98	15	15	"
171.	99	3	3	31
172.	97	16	16	"
173.	99	5	5	72
174.	100	28	28	"
175.	100	6	6	61
176.	99	6	6	19
177.	95	4	4	"
178.	93	8	9	49
179.	99	5	5	51
180.	81	9	11	48
181.	100	7	7	21
182.	98	6	6	33
183.	99	2	2	"
184.	100	17	17	37
185.	100	12	12	"
186.	100	6	6	25
187.	96	7	7	"
188.	87	0	0	29
189.	92	6	7	"
190.	100	7	7	30
191.	100	6	6	"
192.	87	5	6	25
193.	98	9	9	"
194.	100	6	6	52
195.	100	4	4	"
196.	99	15	15	46
197.	82	8	10	23
198.	91	4	4	73
199.	83	3	4	21
200.	84	8	10	"

Nerve No.	F-wave Persistence Value	Repeater F-wave No./100 M waves	%Repeater F-wave Value	Age
201.	87	6	7	53
202.	100	6	6	31
203.	80	8	10	51
204.	89	8	9	30
205.	87	12	14	68
206.	82	13	16	"
207.	70	15	21	63
208.	70	15	21	61
209.	76	6	8	47
210.	96	5	5	57
211.	100	0	0	58
212.	82	4	5	27
213.	95	3	3	"
214.	92	2	2	28
215.	98	4	4	23
216.	100	2	2	"
217.	75	2	3	18
218.	88	6	7	"
219.	90	5	6	51
220.	92	2	2	"
221.	94	3	3	22
222.	98	3	3	"
223.	77	4	5	28
224.	83	11	13	"
225.	86	5	6	21
226.	80	2	3	23
227.	84	11	13	"
228.	95	2	2	64
229.	90	7	8	"
230.	81	3	4	31
231.	89	4	4	"
232.	92	2	2	22
233.	100	3	3	"
234.	100	7	7	51
235.	100	6	6	"
236.	88	10	11	21
237.	92	9	10	68
238.	100	11	11	"
239.	83	9	11	71
240.	96	10	10	"
241.	100	12	12	69
242	78	13	17	"

TABLE 6

F-WAVE PERSISTENCE AS A FUNCTION OF AGE

ULNAR NERVE/ABDUCTOR DIGITI MINIMI
(n = 242)

Age (yrs)	≤25	26 - 35	36 - 45	46 - 55	56 - 65	>65
F-WAVE PERSISTENCE VALUE	84 87 100 98 84 82 90 83 91 84 87 98 95 100 90 75 90 88 99 94 92 98 75 86 61 80 88 84 100 92 30 100 98 88 100 100 98 96 99 95 100 100 96	50 99 91 97 78 98 96 99 78 87 90 92 100 100 100 100 100 100 100 89 85 82 70 95 90 92 94 77 100 83 100 81 95 89 81 61 100 100 83 88 92 83 80 74	80 100 18 97 30 98 100 88 100 100 100 75 100 97 99 100 100 100 100 98 100 100 100 100 93 100 100 93 100 100 97 100 100 90 92 100 100 70 96 53 98	90 100 92 91 81 100 80 100 100 93 98 99 73 81 46 100 89 100 96 99 65 87 94 80 71 76 100 90 93 92 96 100 74 100 100 100 96 100 100 97 100 100 96 100 100 90 100	100 86 90 100 96 70 94 70 70 96 92 100 81 90 100 95 94 95 89 100 100 100 93 100 100 100 64 60 99 96 91 90 96 100 77	80 92 80 100 90 83 95 96 100 100 90 78 100 99 100 99 95 96 100 100 100 95 94 100 99 100 99 100 91 87 82
	n = 43	n = 44	n = 41	n = 47	n = 35	n = 32

TABLE 7

F-WAVE PERSISTENCE AS A FUNCTION OF AGE

MEDIAN NERVE/ABDUCTOR POLLICIS BREVIS
(n = 247)

Age (yrs)	≤25	26 - 35	36 - 45	46 - 55	56 - 65	>65
F-WAVE PERSISTENCE VALUE	60 85 83 83 90 93 65 73 98 70 75 90 82 100 100 50 82 78 74 87 76 86 97 60 94 80 87 76 76 69 97 81 62 85 76 80 90 61 71 70 99 58 98 85 30 67 79 83 60 42 75 15 84 46 100 40 100 90 93	76 87 75 84 72 81 80 94 75 95 70 88 100 78 85 96 87 96 83 91 97 84 100 79 90 82 51 87 81 94 80 100 53 98 73 90 93 100 86 54 98 99 99 83	100 90 100 75 89 94 100 90 88 54 88 80 100 98 95 90 90 90 100 92 100 91 90 94 87 100 92 95 83 100 100 65 81 90 90 100 90 48 90 72 58 100	89 74 60 100 25 75 34 100 80 100 80 91 96 78 92 100 100 93 100 73 67 88 55 80 93 98 88 86 100 90 89 91 99 99	90 86 90 81 90 73 75 100 75 100 100 85 95 89 95 98 68 96 75 100 98 86 94 100 100 92 98 100 91 92 100 91 100	70 53 77 81 80 90 85 83 100 91 100 88 73 76 87 71 66 92 90 91 67 54 90 77 74 77 36 72 70 82 99 100 98 100
	n = 59	n = 44	n = 42	n = 34	n = 34	n = 34

TABLE 8

%REPEATER F-WAVE VALUE AS A FUNCTION OF AGE

ULNAR NERVE/ABDUCTOR DIGITI MINIMI
(n = 242)

Age (yrs)	≤25	26-35	36-45	46-55	56-65	>65
%REPEATER F-WAVE VALUES	10 11 6 17 6 2 14 4 13 9 7 2 3 6 3 3 7 11 5 6 7 9 16 10 4 4 7 10 11 4 21 2 9 2 5 7 10 3 14 3 16 10 12	8 6 5 11 6 13 6 10 4 8 7 5 14 16 7 5 4 3 8 16 0 6 4 2 5 0 23 7 20 7 13 6 0 6 0 9 5 5 5 3 8 2 12 6	19 7 0 7 0 6 6 12 4 26 0 9 6 25 2 26 10 0 4 16 4 33 0 9 6 8 18 17 0 7 6 8 4 11 3 15 7 17 5 12 0	6 0 6 7 4 4 6 14 15 19 12 10 5 10 8 5 0 6 32 5 2 33 3 7 2 12 6 0 11 0 7 16 6 6 13 6 18 18 4 7 4 8 9 14 5 4 11	5 8 2 9 5 21 10 12 14 30 3 14 20 6 8 7 9 21 17 21 0 5 12 0 4 2 0 8 4 20 12 10 0 30 18	5 0 10 4 0 0 2 5 20 28 11 4 3 14 4 16 28 10 5 11 5 11 4 10 12 12 15 17 6 5 17 33
	n = 43	n = 44	n = 41	n = 47	n = 35	n = 32

TABLE 9

%REPEATER F-WAVE VALUE AS A FUNCTION OF AGE

MEDIAN NERVE/ABDUCTOR POLLICIS BREVIS
(n = 247)

Age (yrs)	≤25	26 - 35	36 - 45	46 - 55	56 - 65	>65
%REPEATER F-WAVE VALUE	37 35 5 7 35 15 32 11 16 49 18 22 10 10 16 44 29 24 37 19 4 18 6 7 13 20 21 13 38 5 50 11 10 14 38 19 9 6 24 8 8 30 26 9 7 22 20 8 28 6 11 4 20 24 60 0 32 12 16	3 19 3 16 42 2 8 27 9 26 0 20 0 14 7 23 2 4 17 22 13 4 0 14 6 10 41 26 10 13 0 23 34 0 21 0 6 12 6 5 24 12 6 25	0 60 7 0 13 11 6 28 9 14 2 11 4 48 2 33 6 16 3 27 0 4 9 7 13 10 8 6 24 0 6 4 34 8 27 9 11 6 7 4 16 22	31 4 17 7 24 9 59 10 6 28 0 3 7 4 5 0 5 5 3 8 15 4 4 22 4 11 6 15 6 20 11 17 19 13	3 15 10 19 10 13 7 16 11 3 8 8 17 12 8 12 21 31 13 4 8 29 18 5 5 6 9 13 15 13 7 5 2 7	14 4 29 10 13 5 12 14 8 11 15 21 12 2 44 4 9 8 24 15 9 21 42 9 22 17 17 11 9 10 26 20 13 7
	n = 59	n = 44	n = 42	n = 34	n = 34	n = 34

TABLE 10

THE INFLUENCE OF AGE ON F-WAVE PERSISTENCE IN ABDUCTOR POLLICIS BREVIS AND ABDUCTOR DIGITI MINIMI IN HEALTHY VOLUNTEERS

MEDIAN NERVES

No. of Nerves	Age (Yrs)	F Persistence (No. F-waves/100 M-waves) Mean (S.D.)
59	≤25	76.9 (17.9)
44	26-35	85.1 (12.2)
42	36-45	88.6 (12.6)
34	46-55	84.2 (18.1)
34	56-65	91.2 (9.2)
34	>65	80.6 (14.6)
n = 247		

ULNAR NERVES

No. of Nerves	Age (Yrs)	F Persistence (No. F-waves/100 M-waves) Mean (S.D.)
43	≤25	89.7 (12.5)
44	26-35	98.1 (11.2)
41	36-45	91.8 (18.1)
47	46-55	91.6 (11.5)
35	56-65	91.7 (10.4)
32	>65	93.3 (8.7)
n = 242		

TABLE 11

THE INFLUENCE OF AGE ON %REPEATER F-WAVE VALUES MEASURED IN ABDUCTOR POLLICIS BREVIS AND ABDUCTOR DIGITI MINIMI MUSCLES OF HEALTHY VOLUNTEERS

MEDIAN NERVES

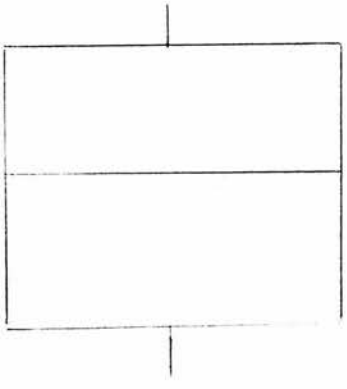
No. of Nerves	Age (Yrs)	% Repeater F-wave Value Mean (S.D.)
59	≤25	19.3 (13.2)
44	26-35	13.1 (11)
42	36-45	12.7 (12.8)
34	46-55	11.8 (11.3)
34	56-65	11 (6.2)
34	>65	14.9 (9.5)
n = 247		

ULNAR NERVES

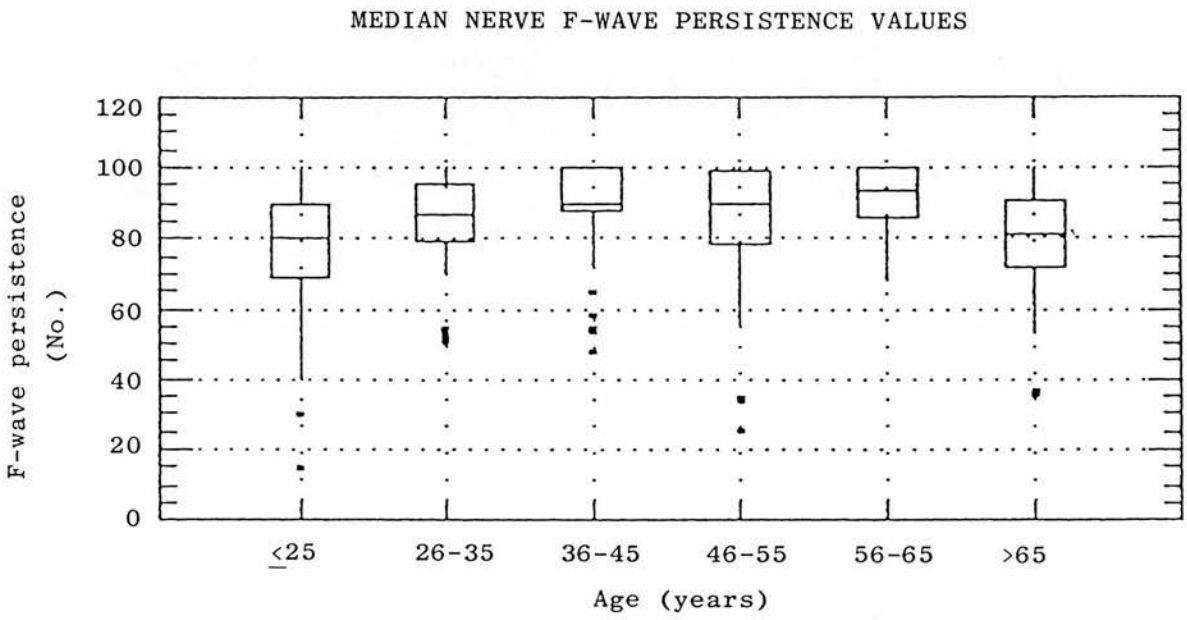
No. of Nerves	Age (Yrs)	% Repeater F-wave value Mean (S.D.)
43	≤25	7.9 (4.6)
44	26-35	7.2 (5)
41	36-45	9.1 (8.1)
47	46-55	8.6 (7.0)
35	56-65	10.5 (8.1)
32	>65	10.2 (8.2)
n = 242		

MULTIPLE BOX-AND-WHISKER PLOTS OF % REPEATER F-WAVE VALUES AND F-WAVE PERSISTENCE VALUES FROM MEDIAN NERVES/ABDUCTOR POLLICIS BREVIS MUSCLES (n = 247) AND ULNAR NERVES/ABDUCTOR DIGITI MINIMI MUSCLES (n = 242) FROM HEALTHY VOLUNTEERS ARE CONTAINED OVERLEAF IN FIGURES 9 AND 10

KEY:-



The plot divides data into 4 areas of equal frequency. The central box covers the middle 50% of data values, between the upper and lower quartiles. The "whiskers" extend out to those values within 1.5 times the interquartile range. Values outwith the range of the "whiskers" are plotted individually. The central line in the box represents the median value.


MEDIAN NERVE F-WAVE PERSISTENCE VALUES
F-wave persistence (No.)
120
100
80
60
40
20
0
≤25
26-35
36-45
46-55
56-65
>65
Age (years)

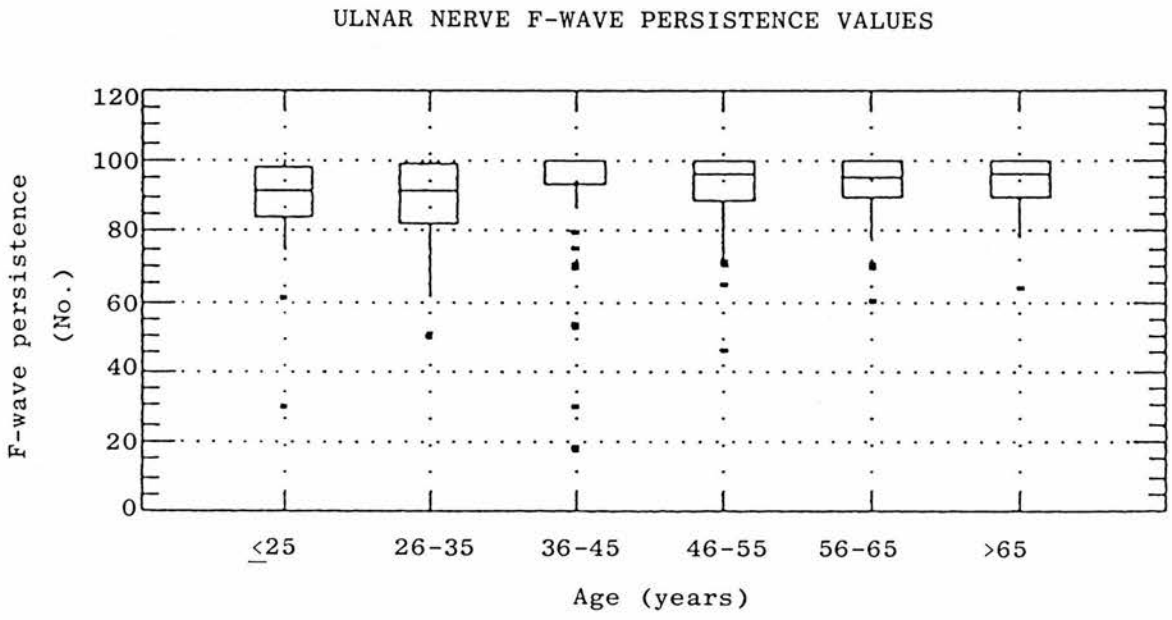

ULNAR NERVE F-WAVE PERSISTENCE VALUES
F-wave persistence (No.)
120
100
80
60
40
20
0
≤25
26-35
36-45
46-55
56-65
>65
Age (years)

FIGURE 9

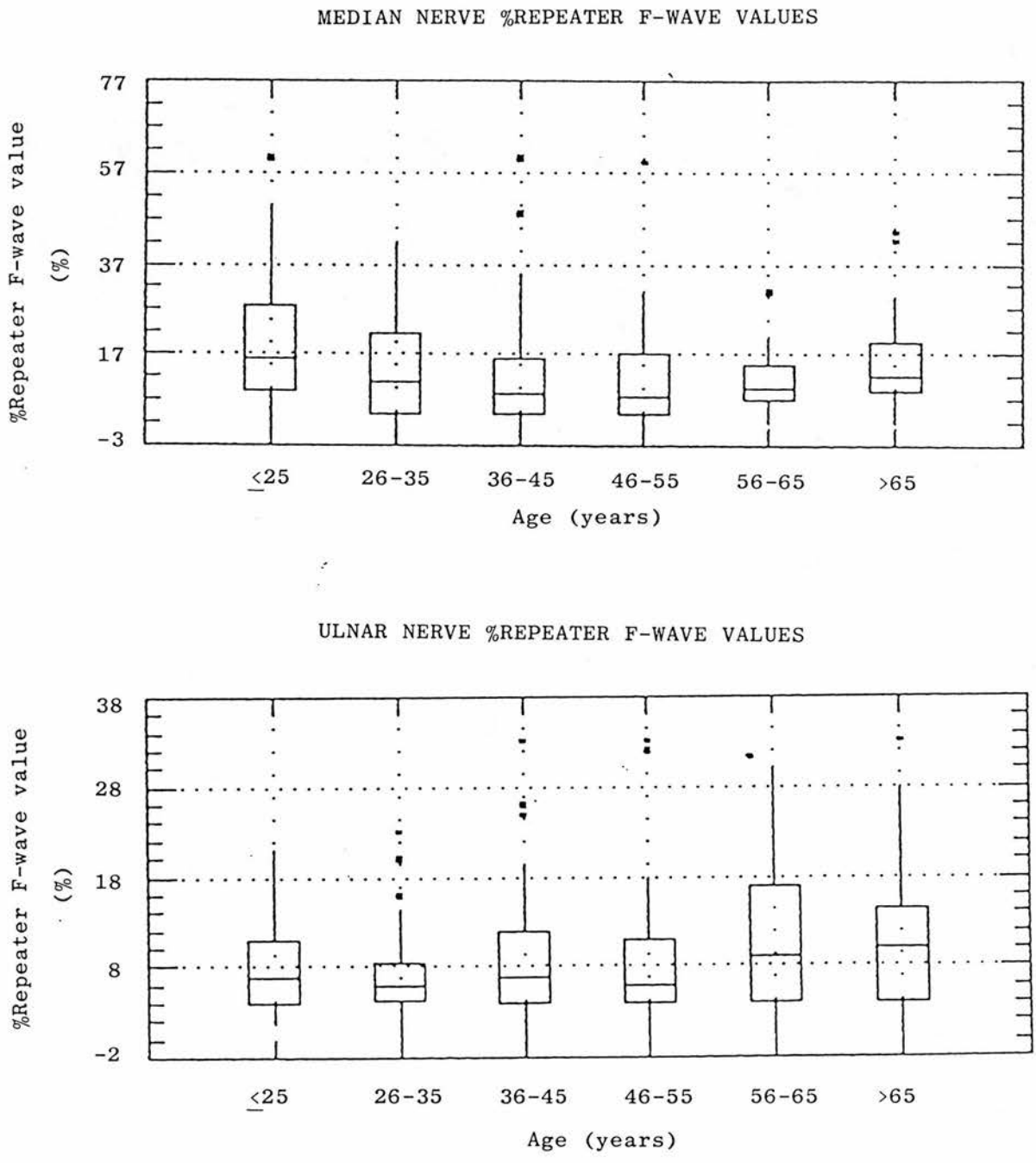

MEDIAN NERVE %REPEATER F-WAVE VALUES
%Repeater F-wave value (%)
77
57
37
17
-3
≤25
26-35
36-45
46-55
56-65
>65
Age (years)
ULNAR NERVE %REPEATER F-WAVE VALUES
%Repeater F-wave value (%)
38
28
18
8
-2
≤25
26-35
36-45
46-55
56-65
>65
Age (years)

FIGURE 10

TABLE 12

STATISTICAL ANALYSIS OF F-WAVE PERSISTENCE AS A FUNCTION OF AGE

MEDIAN NERVES

One-way Analysis of Variance

Source of Variation	Sum of Square	d.f.	Mean Square	F-ratio	Sig. level
Between groups	6035.787	5	1207.1574	5.436	.0001
Within groups	53514.269	241	222.0509		
Total (corrected)	59550.057	246			

Multiple range analysis for F-wave persistence by age

Method Age group (years)	95% Tukey HSD Intervals Count	Average	Homogeneous Groups		
≤25	59	76.881356	*		
>65	34	80.588235	*	*	
46-55	34	84.205882	*	*	*
26-35	44	85.090909	*	*	*
36-45	42	88.547619		*	*
56-65	34	91.147059			*

Multiple range analysis : Outlying values excluded

Method Age group (years)	95% Tukey HSD Intervals Count	Average	Homogeneous Groups		
≤25	57	78.789474	*		
>65	33	81.939394	*	*	
26-35	41	87.463415		*	*
46-55	32	87.625000		*	*
56-65	34	91.147059		*	*
36-45	38	91.947368			*

d.f. = degrees of freedom

TABLE 13

STATISTICAL ANALYSIS OF F-WAVE PERSISTENCE AS A FUNCTION OF AGE

ULNAR NERVES

One-way Analysis of Variance

Source of Variation	Sum of Square	d.f.	Mean Square	F-ratio	Sig. level
Between groups	461.716	5	92.34315	.573	.7206
Within groups	38028.586	236	161.13808		
Total (corrected)	38490.302	241			

Multiple range analysis for F-wave persistence by age

Method Age group	95% Tukey HSD Intervals Count	 Average	Homogeneous Groups
26-35	44	89.068182	*
<25	43	89.651163	*
46-55	47	91.595745	*
56-65	35	91.714286	*
36-45	41	91.756098	*
>65	32	93.250000	*

TABLE 14

STATISTICAL ANALYSIS OF %REPEATER F-WAVE VALUES AS A FUNCTION OF AGE

MEDIAN NERVES

One-way Analysis of Variance

Source of Variation	Sum of Squares	d.f.	Mean Square	F-ratio	Sig. level
Between groups	2226.296	5	445.25928	3.441	0 .0051
Within groups	31183.534	241	129.39226		
Total (corrected)	33409.830	246			

Multiple range analysis for %Repeater F-wave values by age

Method: 95% Tukey HSD Intervals

Age groups (years)	Count	Average	Homogeneous Groups	
56-65	34	11.000000	*	
46-55	34	11.823529	*	
36-45	42	12.738095	*	*
26-35	44	13.090909	*	*
>65	34	14.911765	*	*
≤25	59	19.288136		*

d.f. = degrees of freedom

TABLE 15

STATISTICAL ANALYSIS OF %REPEATER F-WAVE VALUES AS A FUNCTION OF AGE

ULNAR NERVES

One-way Analysis of Variance

Source of Variation	Sum of Square	d.f.	Mean Square	F-ratio	Sig. level
Between groups	322.882	5	64.576450	1.352	.2435
Within groups	11276.159	236	47.780335		
Total (corrected)	11599.041	241			

Multiple range analysis for %Repeater F-wave values by age

Method Age group (years)	95% Tukey HSD Intervals Count	Average	Homogeneous Groups
26-35	44	7.181818	*
<25	43	7.930233	*
46-55	47	8.425532	*
36-45	41	9.146341	*
>65	32	10.218750	*
56-65	35	10.485714	*

F-wave persistence: median nerves

Analysis of variance gave a variance ratio of 5.436 which was significant at a p value of 0.0001, indicating that some of the group means were significantly different. The Tukey multiple range comparison procedure gave results which are open to a number of different interpretations. One of the hypotheses contained in the introduction to the thesis is that peripheral nerve lesions might result in F-wave impersistence. If an age-related change needs to be taken into account when the effects of peripheral nervous system lesions on F-wave persistence are measured, any differences observed at the extremes of the age range are likely, it would appear, to be of most relevance. The physiological changes in the innervation of muscle which might be relevant to this analysis occur in old age (Campbell et al 1973).

The age group with the lowest mean F-persistence value (76.9) (and a relatively large standard deviation) is the group aged $\leq$25 years, and most of the difference producing the high F-value (variance ratio) could be accounted for by the youngest group. In the light of theoretical considerations and the future application of the measurement of F-wave persistence, the difference in the mean of the oldest group of nerves as well as that of the youngest group of nerves compared with the other group means would appear to be relevant. These findings are, therefore, taken to show that in the oldest and youngest groups mean values for F-wave persistence are significantly different from those of the intermediate age groups.

To see what effect the outlying values (beyond the whiskers of the Box and Whisker plots) had on the analysis, the analysis of variance and Tukey test was applied when the outlying values were excluded. For relevant statistical analysis see Table 12. Highly significant differences were still present between some of the group means ($p<0.0001$). In view of the considerations already mentioned concerning the effects of ageing on the

motor neurone pool, the Tukey range test is most appropriately interpreted as showing no significant difference in the means of the groups over the age of 25 and under the age of 66. The means of the youngest and oldest groups are significantly different from those of the intermediate groups.

F-wave persistence: ulnar nerves

The analysis of variance detected no significant differences between the means of each of the six age groups (p=0.72).

%Repeater F-wave values: median nerves

The one-way analysis of variance gave a variance ratio of 3.44 which was significant at a p value of 0.005 indicating that some of the means were significantly different.

The Tukey procedure showed that the under 26 years group had a mean %Repeater F-wave value (19.3%) which was significantly higher than the means of the other groups. No significant difference was found between the mean values of the other five groups when those five groups were compared, one with the other.

%Repeater F-wave values: ulnar nerves

The analysis of variance did not point to a significant difference between the means of any of the groups (p=0.243).

2.4.4. Discussion and conclusions

A significant age-related effect on the two measurements used to quantify F-wave generating behaviour was identified only in the median nerves/abductor pollicis brevis muscles. No significant age-related effect was

seen in the ulnar nerves/abductor digiti minimi muscles. In the median nerves the significant differences in the measurements lay between those in the youngest and oldest groups compared with the intermediate groups in the F-wave persistence measurement, but only between the youngest group and the other groups in the %Repeater F-wave calculation.

The reason for identifying such age effects in the median nerves but not in the ulnar nerves is unclear. It was seen, in 2.2, that there are differences in the patterns of F-wave production, as quantified by the 2 measurements (F-wave persistence and the %Repeater F-wave) between age-matched ulnar and median nerves.

The increase in F-wave impersistence seen in old age in the median nerves tested here suggests that when the effect of pathological lesions on F-wave persistence is being quantified age might reasonably be taken into account.

It should be apparent from the results of experiments described later in the thesis, that a reduction in sensitivity of the diagnostic tests described to quantify F-wave production would result if control/patient comparisons did not include age-matching (in median nerves abductor pollicis brevis). The inclusion of the oldest and youngest age groups into the control range would reduce the sensitivity of these diagnostic tests.

Because of this age-related influence, the investigation into F-wave persistence in 3 different motor neurone pools in Chapter 2 was restricted to subjects aged 26 - 65 years.

CHAPTER 3

CHAPTER 3

"LATE" RESPONSES WHICH MUST BE DISTINGUISHED FROM THE F-RESPONSE

3.1. Introduction

It is essential that when F-response patterns are quantified, for experimental and diagnostic purposes, the recorded "late" responses are, indeed, F-responses and not responses of a different origin falling in the test nerve/muscle's F-latency range. By ensuring that the stimulation/recording paradigm is optimised for the F-response the likelihood of misinterpretation of the obtained responses is diminished. Various experimenters utilising the F-wave, particularly for quantifying motor neurone excitability, have used sub maximal electrical shocks and other investigators have used voluntary contraction of the test muscle to increase the size of the late response and its persistence (Beydoun and Engel 1985). These practices introduce factors which could alter the nature of the recorded late response (see 1.4) (Hagbarth 1962, Upton et al 1971, Schiller and Stålberg 1978). A variety of different "late" response types can be recorded from intrinsic hand muscles and these will be described briefly. The two which can cause confusion, most readily, are the axon reflex and the delayed M component. Ways of differentiating these from F-responses will be considered.

3.2. The H-Reflex

An F-response can be transformed into a "late" response with the characteristics of a reflex discharge under certain circumstances (Hagbarth 1962). In the relaxed state the characteristics of the H-reflex and its anatomical distribution largely preclude confusion with the F-response in the adult. Lloyd (1943(b)) showed that the H-reflex in the cat is a monosynaptic reflex with a rapidly conducting afferent pathway, as had been suggested by Hoffmann (1918). Magladery and colleagues (1951) confirmed, by recording action potentials from dorsal and ventral spinal roots, that spinal transmission was sufficiently rapid for the H-reflex to be a monosynaptic reflex. It is most easily recorded from soleus and has a threshold for electrical stimulation below that of alpha motor fibres. Increments in the stimulus cause the H-reflex to grow until the motor threshold is reached after which further increases in the intensity of the shock progressively block the H-reflex and elicit F-waves (Figure 11). The amplitude of the surface recorded H-reflex can be up to several mV. It can be facilitated by tetanic stimulation of the nerve involved, by voluntary contraction of the test muscle, and by the Jendrassik maneouvre (Hagbarth 1962). The reflex is inhibited by contraction of antagonistic muscles or a conditioning shock preceding the test shock by approximately 40-110 ms (McLeod 1969). In contrast to the F-response, the shape and amplitude of the H-reflex can remain very constant during long periods of stimulation if the relationship between the stimulus and the nerve is fixed. The number and identity of motor neurones involved in the H-reflex can, therefore, be virtually unchanged during a train of consecutive stimuli. The H-reflex's latency is shortened by moving the stimulus proximally and in the triceps surae it falls in a similar latency range as that of the F-response.

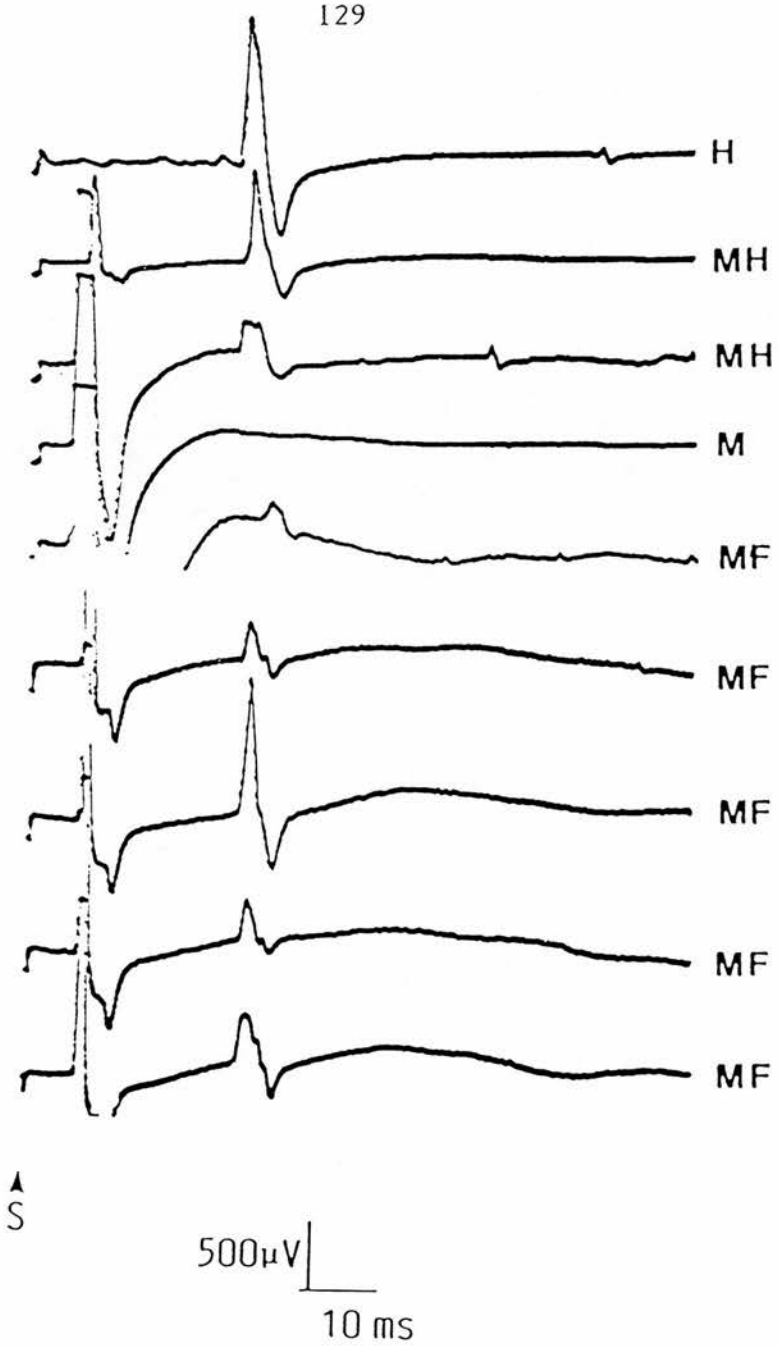


FIGURE 11

"Late" muscle responses recorded from soleus stimulating the posterior tibial nerve in the popliteal fossa. A gradual transition from an H-reflex to an F-response results from increments in stimulus intensity from the uppermost to the lowermost sweep. In the upper 3 sweeps, the H-reflex potential was reproduced by serial stimuli at each stimulus intensity.

H = H-reflex; M = M wave; F = F-wave.

(Stimulus duration 1 millisecond).

The H-reflex cannot usually be recorded from relaxed intrinsic hand muscles of a healthy adult. Under optimised conditions H-reflexes have been reported in the extensor digitorum brevis muscle of healthy adults (Willer 1975). There are other muscles from which an H-reflex can be obtained in healthy adulthood including flexor carpi radialis, masseter, quadriceps and hamstring muscles (Deschuytere and Roselle 1974, Godaux and Desmedt 1975, Deschuytere et al 1976, Jabre 1981, Aiello et al 1983, Ongerboer de Visser et al 1984). The soleus muscle is exceptional because of the ease with which a high amplitude monosynaptic reflex can be elicited during relaxation and, even with the facilitating effect of a voluntary contraction, the gastrocnemii do not contribute significantly to the reflex recorded with surface electrodes over the calf muscle (Hagbarth 1962).

It is possible to change an F-response into a typical H-reflex with a voluntary contraction of the test muscle (see 1.4.3). This effect of a slight or moderate contraction appears to be more evident in thenar and tibialis anterior muscles than in hypothenar and extensor digitorum brevis muscles (Hagbarth 1962).

In some conditions H-reflexes may be recorded from muscles which do not yield H-reflexes in health Pinelli and Valle (1960). Hohmann and Goodgold (1961), Thorne (1965) and Ioku (1984) were able to record "late" responses with the characteristics of H-reflexes from the anterolateral muscles of the lower limb and the small hand muscles of patients with suprasegmental pyramidal tract lesions. Before full maturation of the central nervous system takes place H-reflexes can be detected in the hypothenar muscle as a normal finding (Thomas and Lambert 1960, Hodes and Gribetz 1962).

Changes in the strength of an electrical stimulus used to elicit an H-reflex in triceps surae modify not only the amplitude of the evoked compound muscle action potential but also have an effect on the reflex conduction latency of individual motor neurones which continue to participate in the reflex at different stimulus intensities (Trontelj 1973). The rate of transmission of a reflex discharge through an individual motor neurone is modified by changes in the intensity of electrical stimuli delivered to the peripheral nerve. The considerable latency variability of consecutive H-reflex responses (of up to 2,500 μsecs) contrasts with the small latency variability (usually <100 μsec) of consecutive F-responses conducted by individual motor neurones (Schiller and Stålberg 1978). These studies referred to cite values from different muscles (soleus and abductor digiti minimi) but jitter differences in the same motor neurones for H-reflexes and F-responses have been documented in the facial nerve and allow ready distinction between the two "late" responses (Trontelj and Trontelj 1973).

3.3. V1 and V2

Hagbarth (1962) demonstrated that by voluntarily recruiting motor units in an intrinsic hand muscle, from which "late" responses were being recorded, and at the same time reducing the intensity of the electrical stimulus delivered to the muscle's mixed nerve, the characteristics of the evoked "late" response could be changed from recurrent to reflexive. The F-response evoked by a supramaximal nerve shock may also be modified when a voluntary contraction of the test muscle coincides with the electrical stimulus to the nerve (Upton et al 1971). Upton and colleagues found that when a maximal voluntary contraction was timed to coincide with the shock to the nerve two distinct compound muscle action potentials followed the M wave (see Figure 12). The first fell earlier (by approximately 2 msec) than the earliest F-response and this was termed V1. The second response fell later than the F-response (between 48 and 60 ms in abductor pollicis brevis) and was termed V2. V1 and V2 are recorded only rarely from leg or foot muscles (Iles 1977). The size of V1 and V2 fluctuates from trial to trial and is maximised by increasing the strength of the voluntary contraction. The prominence of V1 diminishes after a sequence of trials and is seen to differ between subjects. It is not, unlike R1 and R2 responses, necessary to average large numbers of sweeps to obtain visualisation of V1 and V2. V1, when recorded from abductor pollicis brevis, can be very prominent and can approach the size of the M wave, unlike the F-wave which is often less than 1 mV in amplitude (peak-peak). A change in the stimulus intensity can further alter V1's configuration: by reducing the stimulus intensity from just supramaximal to just above threshold for the M wave a response larger than the M wave can be obtained. This, and other findings, (shortening of the latency by moving the stimulus proximally and abolition of the response by rhizotomy) indicates V1 has a reflex origin (Upton et al 1971). V1 is

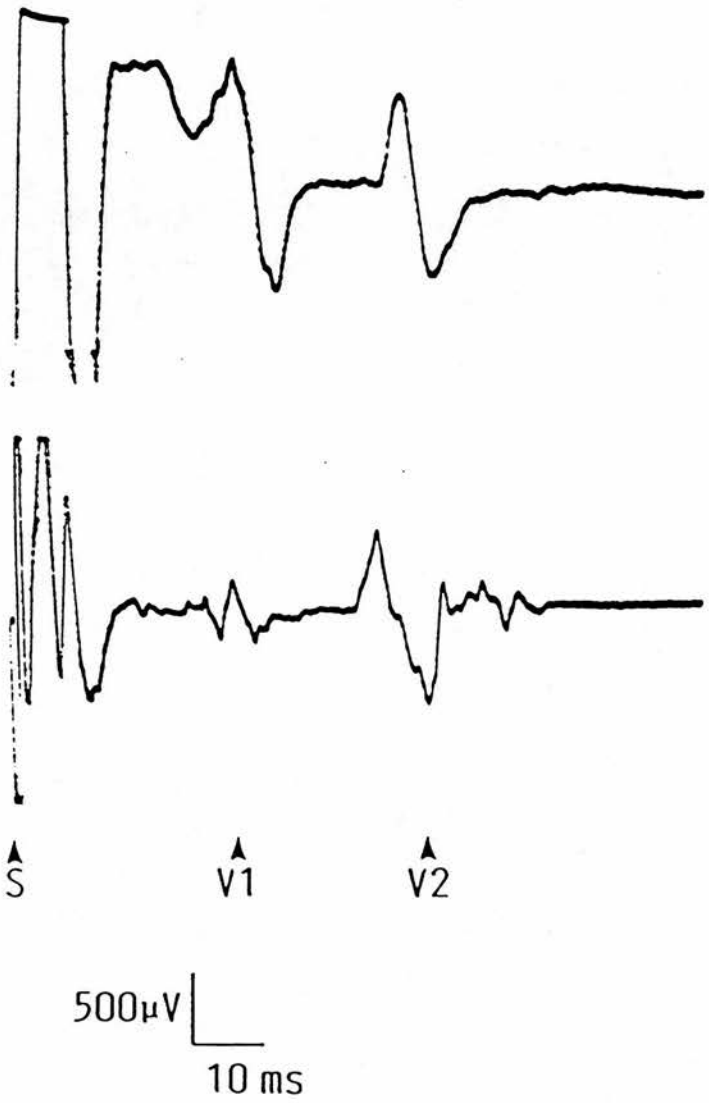


FIGURE 12

V1 and V2 responses recorded from a healthy abductor pollicis brevis muscle during a voluntary recruitment of its motor units. The 2 sweeps shown illustrate the variability of V1 and V2 in time. The stimulus used was an 80V, 1 ms duration pulse.

generated only when motor neurones are adequately facilitated and when lower motor neurones are cleared for transmission of the reflex discharge by collision between antidromic motor impulses and volitional orthodromic motor impulses (Upton et al 1971, Stanley 1978). The collision between volitional impulses and antidromic motor impulses explains the retention of a reflex discharge when a supramaximal shock is delivered to the mixed nerve.

For a supramaximal shock to generate a reflex discharge in adult intrinsic hand muscle, unaffected by a suprasegmental pyramidal tract lesion, the test motor neurone pool requires facilitation and part of the efferent pathway has to be cleared of antidromic impulses. To optimise conditions in which F-responses are less likely to be contaminated by reflex discharges the practice of contracting the test muscle to generate larger and more persistent F-responses has been avoided in the experiments contained in this thesis (Knezevic et al 1985). Conractions of different strengths would have differing effects on the excitability of a test muscle's spinal motor neurones. Even if a voluntary contraction is monitored and maintained at a steady force, the effects of this maneouvre on the excitability of the test motor neurone pool is likely to be extremely complex and inter-subject variation might be considerable. The variables induced by contracting a test muscle while recording F-waves have, in the experiments in this thesis, been minimised by attempting to stimulate and record while the subjects' muscles are relaxed. The effects of sensory fibre stimulation (e.g. spindle afferents) during F-wave recording will be mentioned in the section which considers the effects of peripheral nervous system lesions on F-wave persistence and %Repeater F-wave values (4.3).

3.4 R1 and R2

Eisen and his colleagues used shocks, unlike those conventionally used to generate F-waves, which favoured selective activation of low threshold afferents to generate "late" muscle responses which were termed R1 and R2 (Eisen et al 1984). In those experiments only a weak voluntary muscle contraction was used to facilitate reflex discharges and, unlike the method of Upton and colleagues used to generate V1 and V2, large numbers of sweeps had to be averaged before R1 and R2 could be visualised. These responses seem to have similar latencies and may have the same underlying mechanisms as V1 and V2.

R1 and R2, so named because of their reflex nature, are recorded from abductor pollicis brevis (among other muscles) only under conditions which are optimal for the transmission of reflex volleys.

Unlike soleus, from which a monosynaptic reflex can be recorded immediately after an acute upper motor neurone lesion, (suggesting that the excitatory post synaptic potentials from that muscle's Ia fibres are relatively powerful) it is only by facilitating motor neurones, preferentially activating low threshold afferents, and/or by clearing impulses from motor axons that potentials of a reflex origin can be recorded in the small hand muscles in health (Weaver et al 1963, Garcia-Mullin and Mayer 1972).

3.5. The Axon Reflex

Roth distinguishes two kinds of axon reflex in the upper limb on anatomical grounds (Roth 1979). In one type the two branches of the axon belong to the same anatomical pathway and terminate in the same muscle. In the other type the two branches separate at a bifurcation in the brachial plexus or mixed nerve and pass into separate muscles. This second form has to be actively sought in the electrophysiological examination and could not be confused with an F-response. The first type of axon reflex shares some characteristics with the F-response as both are "late" muscle action potentials which are evoked by a stimulus to the muscle's nerve which exceeds the threshold for alpha axon activation. Both can fall in the same latency range, although the axon reflex appears most commonly at latencies intermediate between those of the M and F-response (Fullerton and Gilliatt 1965). Axon reflexes whose latencies exceed the usual F-wave latency range are not uncommon and Roth found as many as one-third of axon reflexes have latencies in excess of the F-wave latency range for that test nerve/muscle in health (Roth 1979).

The expansion of single motor unit territory which occurs in muscles recovering from partial denervation has been studied with techniques which permit the identification of potentials arising from a single unit in different areas of the muscle (Buchtal et al 1959). More recently, single fibre electromyographic studies have allowed identification of motor unit enlargement by measurement of fibre density (Stålberg and Thiele 1975). The anatomical basis of this incorporation of muscle fibres into functional motor units from effete motor units is variable. Collateral sprouting of intact intramuscular motor fibres close to their terminations was first shown histologically in partially denervated animal muscle (Edds 1953), and several years later, collateral sprouting of motor axons was demonstrated in human

muscle (Coërs 1955, Wohlfart 1955). The existence of more proximal branching of regenerating nerve fibres was shown in work on rabbits where branching was identified at the level of a segmental nerve crush (Shawe 1955). It is not clear how often axon reflexes are conducted through collateral sprouts off healthy motor axons or through regenerated forked axons.

The model of the axon reflex constructed by Fullerton and Gilliatt (1965) to explain their electrophysiological findings in partial denervation is illustrated diagramatically in Figure 13. A weak shock to the nerve distally (e.g. ulnar nerve at the wrist) can selectively depolarise one of the two branches of the axon under the stimulator. As well as the impulse passing directly to the muscle (only a small action potential (M) is recorded due to the distance of the recording needle electrode from the muscle fibres supplied by that branch) an antidromic impulse propagates up to the branch point from where it is conveyed distally in the second branch to activate its muscles fibres. This "late" response, whose latency is dependent on the distance travelled and conduction velocity, is called an axon reflex (A.R.). The effects of increasing the stimulus intensity are described in Figure 13.

In contrast to the variable latency, amplitude and waveform of the F-response, the axon reflex has a constant configuration and appears at a fixed latency in response to an unchanging stimulus (Fullerton and Gilliatt 1965, Trontelj and Trontelj 1973, Roth 1979). The waveform of an axon reflex is unaltered by moving the stimulus to different sites over the length of the limb as long as it remains distal to the bifurcation point of the axon. Increments in the stimulus intensity will have no effect until, at a crucial level, the axon reflex suddenly disappears (when recorded with surface electrodes). When recorded with an appropriate needle electrode (Figure 13) the stronger shock (exceeding a critical intensity) is seen to shorten the

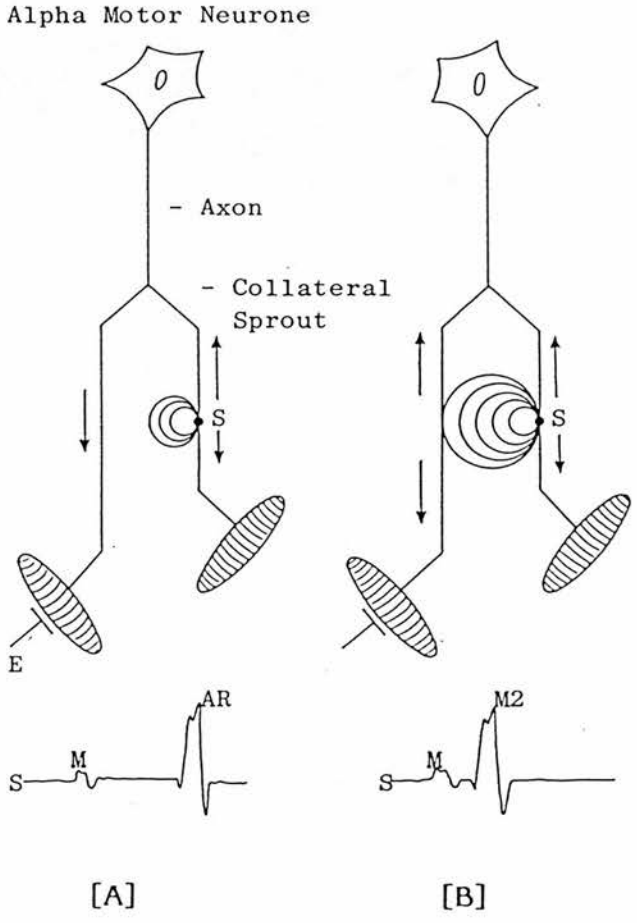


FIGURE 13

DIAGRAMMATIC REPRESENTATION OF THE EFFECT OF INCREASING STIMULUS INTENSITY ON AN AXON REFLEX
(after Fullerton & Gilliatt 1965)

In [A] an axon reflex is recorded (AR): A low intensity electric shock depolarises only the collateral sprout inducing: 1) an antidromic impulse which, at the bifurcation, is conducted distally to depolarise muscle fibres (AR) near the recording electrode (E), 2) propagation of an orthodromic impulse which is detected as a small muscle action potential (M) by the distant recording electrode (E). In [B] the stimulus is made stronger and both axon branches distal to the birfurcation are depolarised. The antidromic impulses collide. The latency of the potential which was previously an axon reflex (now an M wave, M2) is shortened.

S = stimulus; E = needle electrode; M = M wave; M2 = M wave conducted orthodromically in the longer axon branch activated directly; AR = axon reflex potential.

latency of the same muscle potential obtained with a weak stimulus rather than abolish it (the axon reflex becomes an M response). This is due to direct activation of the second nerve branch by the stronger stimulus. A second identical potential does not follow this stronger shock as antidromic activity is present in both limbs of the bifurcation and a collision causes mutual extinction of impulses.

Importantly, axon reflexes have not been found in the intrinsic hand or foot muscles of healthy volunteers (Fullerton and Gilliatt 1965, Gilliatt 1966, Roth 1979). Stålberg and Trontelj (1970), however, found axon reflexes in the medial head of the gastrocnemius muscle in healthy human volunteers and in one case found a branch point 15 cm proximal to the muscle. Axon reflexes have also been demonstrated in the muscles of facial expression of healthy subjects and, surprisingly, evidence of intracerebral branching of facial axons has been found in some instances (Trontelj and Trontelj 1973).

The liability of axon reflexes to be detected in different disorders affecting the lower motor neurone is of interest and relevance. It would appear, from a number of mutually supporting studies, that axon reflexes are detected in a minority of muscles affected by partial denervation and that the duration of the denervating process is crucial in determining the likelihood of detecting axon reflexes (Fullerton and Gilliatt 1965, Sawhney and Kayan 1970, Roth 1979). Roth (1979) showed that axon reflexes occur with a low prevalence in primary disorders of the anterior horn cell, e.g. poliomyelitis and motor neurone disease. They may certainly be present once a neuronopathy has evolved, presumably after the passage of sufficient time has allowed regeneration to occur and connectivity to be established between a nerve branch and the target muscle fibre (Perfetti and Lorizio 1967). Axon reflexes may be found in as few as 10% of patients with chronic denervating neuropathies and tend to occur most commonly in certain forms

of neuropathy; notably Charcot-Marie-Tooth syndrome, hereditary neuropathy with a liability to pressure palsy, and chronic ulnar nerve lesions at the elbow (Roth 1979).

The motor conduction velocity in the afferent and efferent limbs of the axon reflex can be calculated. This has shown that the antidromic impulse is not conducted as far proximally as the spinal cord (when the axon reflex is recorded from the hand), and that the site of the branching is often distal to the nerve lesion. Additionally, the branch with the lower conduction velocity and higher electrical threshold can be activated with a weak stimulus which may fail to activate the nerve branch with the lower threshold of excitation (Fullerton and Gilliatt 1965). The lack of a synaptic connection in its pathway allows the axon reflex to follow repetitive stimulation rates of up to 40 Hz. The branch point of the axon conducting an axon reflex can be localised by finding that the reflex is abolished when the nerve stimulus is applied proximal to the branch point. The effects obtained on a highly persistent individual Repeater F-wave by moving the nerve stimulus more proximally will be shown in Chapter 4.

Trontelj and Trontelj (1973) have studied axon reflexes using a single fibre electromyographic needle. They recorded complex potentials with latencies intermediate between those of the M wave and reflex components which were sensitive to changes in stimulus strength. At a critical stimulus intensity increments or reductions in intensity around that level produced an alternation of direct and "late" responses of intermediate latency in the same muscle fibres. Weaker stimuli produced the intermediate responses, exclusively, while stronger stimuli produced only the early responses. Both responses were never recorded after a single stimulus and the later of the two responses showed a similar jitter to the direct response. By moving the stimulus more proximally it was possible to localise a branching point and

from all these features Trontelj and Trontelj (1973) confirmed the mechanisms involved in the production of the axon reflex which had been suggested by Fullerton and Gilliatt.

Several key differences exist between axon reflexes and F-responses. In particular the axon reflex retains a stable latency and configuration with serial stimuli. The axon reflex is extinguished (when recorded with a surface electrode) by high intensity shocks which optimise the likelihood of generating an F-response. In most instances stimuli can be applied proximal to the branch point so activating the efferent and afferent limbs subserving the axon reflex, in which case the reflex is lost (to surface electrodes). In contrast, the F-response does not disappear as the stimulus is advanced proximally (although the M wave may need to be "collided out" to demonstrate the presence of the F-wave). There are (as far as the author can determine) no descriptions in the literature of responses of intermediate latency, fulfilling the criteria of axon reflexes, which appear intermittently under stable stimulating conditions. This is an important aspect of the axon reflex which is particularly relevant to the studies on the persistence of identical F-responses which are contained in this thesis' experiments.

3.6. Ephaptic Transmission

Lesions in peripheral nerves could result in the formation of pathological "connectivity" between adjacent nerve fibres which might, theoretically, result in the genesis of "late" muscle responses which resemble F-waves.

An impulse propagated in one nerve fibre can modify the excitability of adjacent fibres as was shown by the experiments of Jasper and Monnier (1938) on crab axons. In health, the effects of an impulse passing in one nerve fibre on the excitability of adjacent nerve fibres are minimised by the impedance of intervening tissues. Interactions between active and resting nerve fibres may be relevant to some of the "late" responses recorded from damaged nerves analysed in Chapters 4, 5 and 6.

Arvanitaki (1942) created an artificial synapse between fibres in a squid nerve which she called an 'ephapse'. In this experimental model she was able to induce propagation of an action potential in a resting nerve fibre by transferring current from an active nerve fibre across the 'ephapse' (the response in the receiving fibre was adequate to set up a propagated impulse only after sensitisation by decalcification).

Experimental work on crab axons by Katz and Schmitt (1940) showed that activity in a non-myelinated nerve fibre had subliminal effects on the excitability of an adjacent axon. Jasper and Monnier (1938) found that when impulse transmission was induced experimentally (under certain circumstances) in resting fibres by activity in contiguous axons it occurred at the artificially established point of contact after a long delay (Ca. 20 ms). Whether ephaptic transmission is responsible for some or any of the "late" responses recorded from the pathological material detailed in this thesis is unknown.

3.7. Delayed M Components

Slowed motor conduction can result in temporal dispersion of impulses such that latest M wave components can have their onset in the latency range for that muscle's F-responses.

Figure 14 provides an example and shows how repositioning the stimulating electrode more proximally lengthens the "late" potential.

The shortening of F-response latencies which result from moving the stimulus proximally is illustrated in Figure 25, page 206. This is a simple method of distinguishing between a highly persistent individual Repeater F-wave and a "late" M component.

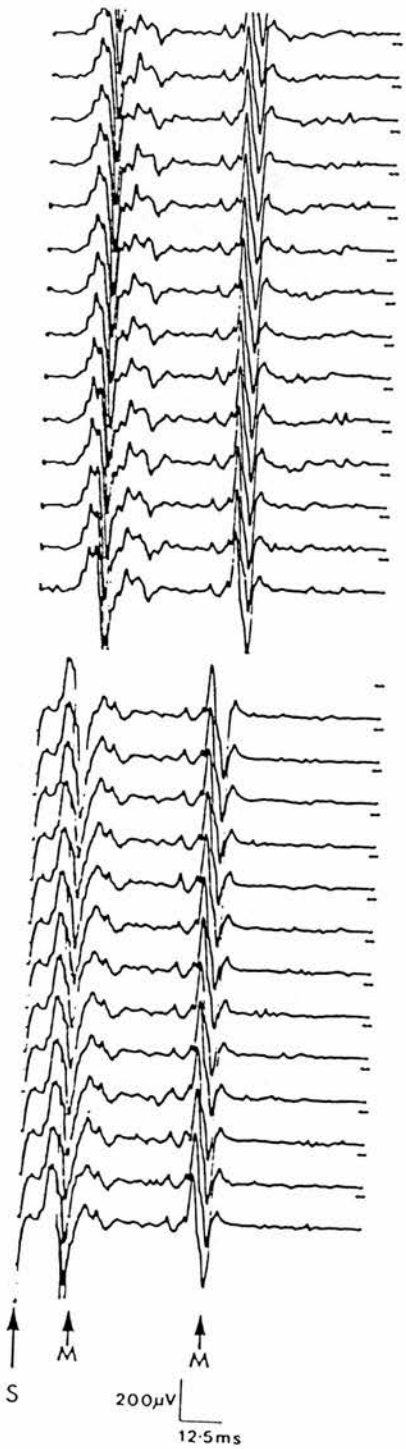


FIGURE 14

Delayed M component recorded from the abductor pollicis brevis, stimulating the median nerve A, at the elbow and B, at the wrist.

CHAPTER 4

CHAPTER 4

ELECTRODIAGNOSTIC AND EXPERIMENTAL APPLICATIONS OF THE F—RESPONSE

4.1. The Utility and Limitations of the F-wave in Present Day Electrodiagnosis

4.1.1. Introduction

This chapter is concerned with both current and new applications of the F-response in clinical neurophysiology.

The various ways of applying F-wave latency measurements to localise lesions in the peripheral nervous system, such entrapment or traumatic lesions of mixed peripheral nerves, will be illustrated.

The neurological disorders in which F-wave measurements have been used diagnostically will be reviewed, in the course of which, the drawbacks, limitations and advantages associated with the use of the F-response in the electrodiagnosis of these conditions will be highlighted.

The experimental uses which have been found for the F-response will be discussed.

Data will be presented which shows that the analysis of F-wave discharge patterns can be used to identify peripheral nerve dysfunction. This forms the basis for a new electrodiagnostic technique.

Finally, some observations and comments on F-wave abnormalities in the Miller-Fisher syndrome will be made.

4.1.2. Identification and localisation of focal peripheral nervous system lesions: General principles

F-responses recorded from different muscles in one or more limbs can be used to localise lesions in the motor pathways of the peripheral nervous system. The concept behind the method is analogous to that of the electromyographic examination. The two techniques, electromyography and F-wave analysis, can be complimentary, but in some cases only one of the two may be applicable or yield diagnostic information. The F-wave is particularly useful when motor conduction block or slowing of motor conduction is present without associated axonal degeneration. Even when the connectivity between lower motor neurone and muscle fibre is lost fibrillation potentials and positive sharp waves may not appear for several weeks, the time of their onset depending on the distance of the muscle from the neural lesion (Lenman 1975). While F-wave latency abnormalities can precede electromyographic abnormalities in some instances, the use of F-wave measurements is anatomically restricted as the F-response cannot be recorded in proximal upper limb muscles, such as supraspinatus, when a supramaximal shock is delivered to Erb's point (as the F-wave is buried in the M wave). The use of the F-wave in the upper limb is limited to evaluation of the motor supply of hand and forearm muscles. Electromyography is, of course, particularly useful in the investigation of proximal wasting and weakness and the two techniques can be complimentary. The detection, by EMG, of denervation potentials in muscles not clinically affected is of particular use in localising lesions, e.g. in a patient with winging of the scapula, the detection of subclinical denervation in the

rhomboid discloses that the lesion is not confined to the motor fibres in the long thoracic nerve of Bell.

Ideally, nerve entrapment syndromes should be detected before the lesion advances to produce denervation, and in some instances F-wave latency measurements give a positive result when electromyography does not (Muhlau et al 1984).

When F-waves can be recorded from different muscles supplied through different branches of the same mixed peripheral nerve, it is possible to detect and localise a lesion, using F-responses alone, and plan treatment before axonal degeneration has developed. Several examples will be considered briefly for illustrative purposes. The median nerve may be compressed under the ligament of Struthers producing a clinical picture similar to that of the anterior interosseous nerve syndrome (Goodgold 1974). F-wave latency analysis may help locate the lesion. If the lesion is confined to the anterior interosseous nerve F-responses from pronator quadratus and/or flexor pollicis longus may be delayed, while those recorded from abductor pollicis brevis would be normal. If, alternatively, F-response latencies recorded from thenar eminence, as well as from muscles supplied by the anterior interosseous nerve, were abnormal, a lesion proximal to the origin of the anterior interosseous nerve (e.g. under the ligament of Struthers) would be suggested. (The possibility of a pronator syndrome remains). An illustrative case report follows: PL, a 30 year old female, evaluated by the author (Massachusetts General Hospital No. 240/52/40) had been unable to extend her right elbow beyond 115° after a fracture at the elbow in childhood. She had an orthopaedic procedure to increase the range of extension at the elbow and immediately post-operatively was found to have impaired pinch grip in her right hand and complained of weakness in her wrist. She was referred to the EMG laboratory nine months later, in

1986, when both electromyography and F-wave studies of median innervated muscles pointed to an anterior interosseous nerve lesion which had been sustained intra-operatively (see Table 16). For accuracy, it is best to record the F-responses using a needle electrode from the equivalent muscle of both limbs and compare latencies recorded in an identical manner from the test limb and the contralateral asymptomatic limb. In the case illustrated, the minimal F-wave latencies and F chronodispersion abnormalities are clearly pathological (c.f. abductor digiti minimi values: a more distal muscle) and comparison with the asymptomatic limb is superfluous.

ELECTROMYOGRAPHY				
Right Upper Limb	High frequency discharges	Denervation	Reinnervation	Reduced motor unit recruitment
Abductor pollicis brevis	-	-	-	-
Pronator quadratus	+	+	+	+
Flexor pollicis longus	-	+	+	+
Flexor digitorum profundus (median head)	-	-	+	+
Flexor digitorum superficialis	-	-	-	-
Pronator teres	-	-	-	-

Right Upper Limb	F-WAVE LATENCIES (ms)
Abductor digiti minimi	26-28
Abductor pollicis brevis	26-27
Flexor pollicis longus	30-37
Pronator quadratus	34-41

+ = present
- = absent

TABLE 16

In the tarsal tunnel syndrome right/left comparisons between the F-wave latency values obtained from abductor digiti quinti and flexor hallucis brevis can be useful. Delayed F-waves to both muscles in one symptomatic foot, associated with "normal" F-wave latencies to the ipsilateral soleus and contralateral small muscles of the foot, would be highly suggestive of a lesion affecting motor fibres at the tarsal tunnel level. If symptoms are confined to the territory of either the medial or lateral plantar branches of the tibial nerve, F-wave latency abnormalities may be confined to the muscles supplied by the affected branch.

Entrapment syndromes and traumatic lesions, e.g. of the radial nerve, the posterior interosseous nerve, the sciatic nerve, (both the deep peroneal and superficial peroneal nerves and the tibial nerve) and the ulnar nerve can be studied using F-wave recordings (Shahani et al 1980(b)). Despite a thorough clinical history and examination the clinician may be left uncertain as to the site of a motor fibre lesion in some cases. For example, a patient with rheumatoid arthritis with weakness and/or wasting of the intrinsic hand muscles may have pain and deformity in the hand and at the elbow suggestive of a lesion of the ulnar nerve either in the cubital tunnel, in Guyon's canal, or at both sites. Rarely, in the cubital tunnel syndrome, motor nerve fibres can be damaged while sensory nerve fibres are spared (Miller 1979). In this setting the retention of a satisfactory sensory potential from the dorsal cutaneous branch of the ulnar nerve is useless in the localisation of the suspected ulnar nerve lesion (Jabre 1980). The placement of the lesion can rest on the pattern of motor fibre dysfunction. F-wave analysis in this example could be useful. If, for example, F-waves recorded from flexor carpi ulnaris, as well as those of intrinsic hand muscles, are pathologically delayed, the proximal site should be considered the more likely. If F-wave latency abnormalities were found in the intrinsic hand muscles, confirming

the presence of dysfunction in the C8,T1 motor fibres to abductor digiti minimi, the finding of normal latency F-responses from flexor carpi ulnaris would be unhelpful as a lesion in the cubital tunnel could spare those fibres. The position of motor axons in peripheral nerve trunks predisposes the motor nerve supply of particular muscles in an entrapment to earlier damage than others which are less susceptible. An example of this is the relative sparing of lumbrical motor fibres in advanced median nerve entrapments (Brown and Yates 1980).

4.1.3. Guillain-Barré syndrome

Lesions have been identified histologically at various sites along the peripheral nerve, from the radicular to the terminal portion of the motor nerve, in the Guillain-Barré syndrome (Asbury et al 1969). Until F-wave measurements were included in the neurophysiological evaluation of patients with idiopathic polyneuritis it was common for conventional nerve conduction studies to give normal results, particularly in the early stages of the illness (Lambert and Mulder 1964, Humphrey 1964). More recently, F-wave studies have suggested that proximally placed lesions can go undetected when only distal segment motor conduction velocity is measured (Kimura and Butzer 1975).

In some patients the only electrophysiological abnormality seen at any time in the course of paresis is a delay in the F-wave latency or excess F chronodispersion (Lachman et al 1977, Lachman et al 1980). Delayed F-responses may aid in the correct diagnosis of the syndrome at a point when cerebrospinal fluid protein content is not elevated and sequential studies are particularly useful in detecting subtle latency changes (Shahani and Sumner 1981). In some cases complete ablation of the late response occurs in the early phase of the illness, even when the M wave from the same

muscle remains within normal limits (for latency and amplitude). Figure 15 illustrates the loss of the F-response in a patient who also had distal conduction block reducing the size of the M response evoked with the stimulus at the wrist. Clinical improvement may be associated with an increase in the amplitude of the compound muscle action potential and reappearance of previously absent F-responses (Shahani et al 1980(a)).

The use of the F-ratio and calculation of the F-wave conduction velocity can be used to determine the presence of slowed conduction in the proximal segment of motor axons innervating hand, forearm, foot and calf muscles (Kimura and Butzer 1975, King and Ashby 1976, Kimura 1978(b)). Motor fibre dysfunction proximal to the axilla can be identified if a stimulus delivered to the ulnar or median nerve at the axilla elicits F-waves in the intrinsic hand muscles which are clearly separated from the M wave (Kimura and Butzer 1975). Less dramatic slowing of motor conduction can be identified by calculating the F-wave conduction velocity over the proximal segment (Kimura and Butzer 1975). Conduction abnormalities usually affect both proximal and distal segments of the motor fibres in Guillain-Barré syndrome, often sparing the elbow-wrist segment in the upper limb (Kimura and Butzer 1975). In these cases a marked increase in terminal latency can balance a proximal latency increase leaving the F-ratio at unity. When this happens slowed motor nerve conduction velocity over the forearm or calf segment associated with a normal F-ratio points to an additional proximal lesion. If axonal degeneration ensues F-response amplitudes and durations may ultimately reflect the process of reinnervation with an expansion of motor unit territories. The assumptions and difficulties implicit in calculating F-wave conduction velocity and the F-ratio are discussed in 2.1.

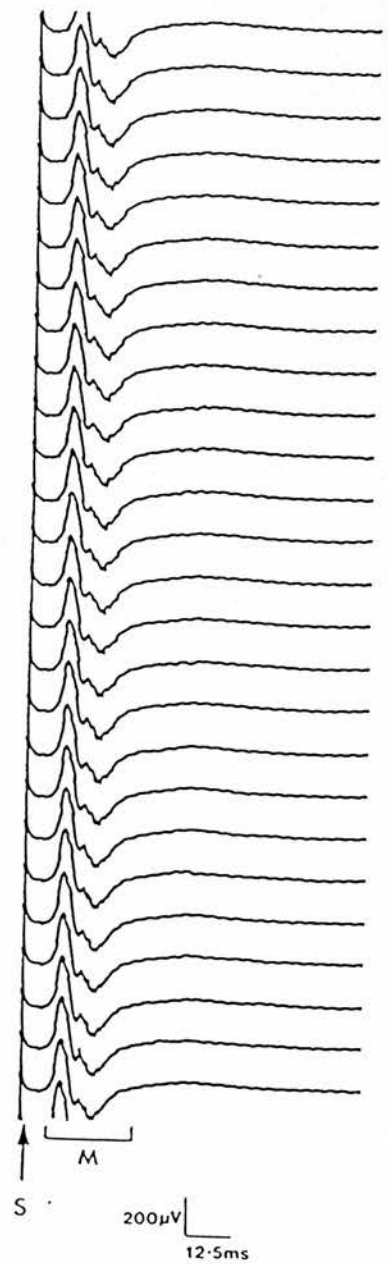


FIGURE 15

F-wave ablation in the paretic abductor digiti minimi of a patient with Guillain-Barré syndrome.

The M wave is pathologically small and the distal motor latency is prolonged (stimulus at the distal skin crease of the wrist).

4.1.4. Peripheral neuropathy

Both minimal F-wave latency and F chronodispersion provide sensitive methods for identifying peripheral neuropathy (Kimura 1974, Panayiotopoulos and Scarpalezos 1976(a), Panayiotopoulos and Scarpalezos 1977, Panayiotopoulos 1978(a), Panayiotopoulos 1979, Lachman et al 1980, Shahani et al 1980(a)). A muscle's minimal F-wave latency can be unequivocably delayed and F-latency values pathologically dispersed when conventional motor and sensory nerve conduction values remain within normal limits. Either or both abnormalities have been documented in chronic peripheral neuropathies with different pathophysiological mechanisms including diabetic, uraemic, porphyric and alcoholic/nutritional types (Mayer and Feldman 1967, Conrad et al 1975, Panayiotopoulos and Scarpalezos 1977, Panayiotopoulos 1978(a), Lefebvre D'Amour et al 1979, Kimura et al 1979, Panayiotopoulos 1979, Panayiotopoulos and Lagos 1980, Shahani et al 1980(a), Ackil et al 1980, Peioglou-Harmoussi et al 1987(b)). Abnormalities of F-responses have been demonstrated in both the primary "axonal" type as well as the segmental demyelinating types of neuropathy. In conditions in which large sensory fibres are specifically damaged, such as Friedreich's ataxia and pure pansensory neuropathy, F-response latencies remain normal while H-reflexes and tendon jerks are absent (Mayer and Feldman 1967, Adams et al 1973). By using F-response latencies to calculate motor conduction velocity in the proximal segment of a mixed peripheral nerve proximal conduction abnormalities can be identified in some diabetic patients while distal segment motor nerve conduction velocity remains normal (Panayiotopoulos 1978(a)). Measuring F-wave impulse velocity along the proximal segments of the peroneal nerve Panayiotopoulos and Scarpalezos 1976(c), Panayiotopoulos (1978(b)) were able to document the involvement of motor nerve fibres in myotonic dystrophy.

The reasons behind the increased sensitivity of F-response latency measurements compared with that of conventional orthodromic sensory conduction and motor conduction in detecting peripheral neuropathy are not well defined. The sensitivity may, in part, be due to the detection of accumulated conduction delays in affected motor fibres. If mild slowing is present diffusely along the length of the motor fibres transmitting F-waves the chance of identifying such marginal dysfunction is proportional to the length of the nerve under test. A more distal stimulus may, therefore, increase the detection rate of such an abnormality compared with the use of a more proximal one. One reason for the relative insensitivity of motor nerve conduction velocity as a measurement for detecting motor fibre lesions is the wide range of values obtained from a healthy population (Kimura 1983). A drop in conduction velocity of 10 m/s, due to a pathological process, could still leave the measured value within the "normal" range. The "normal" range for F-wave latency is narrow, particularly in the nerves/muscles of the hand (compared with the foot), and this may be relevant to its sensitivity (Shahani et al 1980(a), Shahani et al 1980(b), Shahani and Sumner 1981, Kimura 1983, Peioglou-Harmoussi et al 1985(a)). The sensitivity of the F-wave latency measurement in the detection of motor fibre dysfunction may also be related to the population of fibres involved in transmitting the F-wave with the shortest conduction latency. There is evidence to suggest that the earliest conducted F-response is transmitted in the fastest alpha axons (Kimura et al 1984, Shahani et al 1987). If a select subpopulation of the fastest conducting motor neurones is involved in the genesis of the shortest latency F-waves (and this is speculative), then a partial lesion affecting only those motor fibres could, theoretically, have a more significant impact on F-wave latency than on motor nerve conduction velocity as residual intact large motor fibres could permit a normal

measured motor conduction velocity but fail to conduct minimal latency F-responses. The number of test antidromic stimuli used to measure the F-response latency range is also relevant, as a small number may fail to activate an F-wave discharge through one of a reduced number of fastest conducting axons. The true importance of these factors to the sensitivity of the F-wave in detecting lesions is unclear.

Any neuropathic process which affects the proximal segment is more likely to be detected by a test which measures conduction latency across the proximal segments, e.g., diabetes mellitus (Panayiotopoulos 1978(a), Kimura et al 1979, Chokroverty 1980). Another part of the disordered neurone which the F-response tests is the soma. Whether or not the "turnaround" time in the anterior horn cell is increased by processes which result in peripheral neuropathy is unknown, but it has been proposed as an additional mechanism underlying the sensitivity of F-wave latency in the detection of peripheral nerve lesions (Lachman et al 1980). Other F-wave parameters such as the F-wave amplitude and F-wave persistence have not been studied systematically in peripheral neuropathy. F chronodispersion data from only a very small number of healthy and diseased nerves have been published (Panayiotopoulos and Scarpalezos 1976(a), Panayiotopoulos 1979, Shahani et al 1980(a)).

4.1.5. Hereditary sensori-motor neuropathies

Extreme prolongations of F-wave latencies (>3 times the average latency in control subjects) can be found in patients with Type I hereditary sensori-motor neuropathy (Panayiotopoulos 1978(b)). Figure 16 shows very delayed F-responses recorded from the foot muscle of a 25 year old with type I hereditary sensori-motor neuropathy.

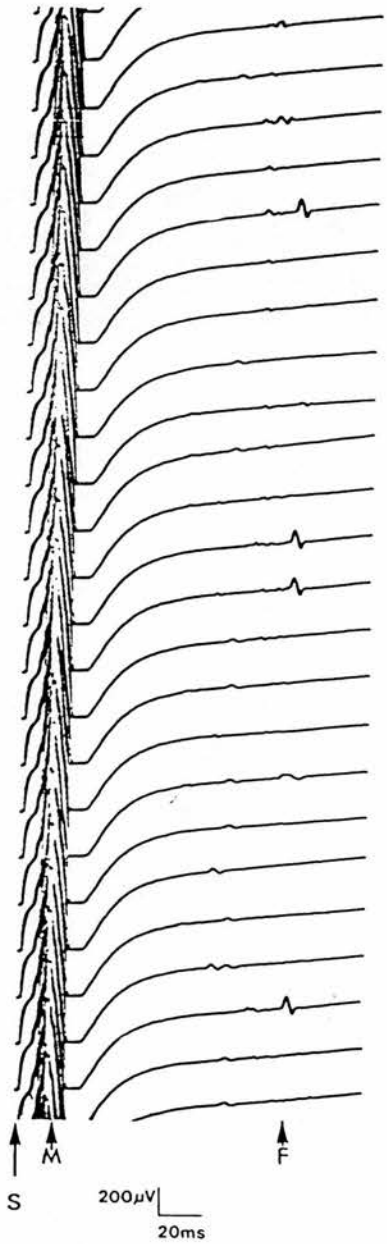


FIGURE 16

CHARCOT-MARIE-TOOTH SYNDROME

Very delayed F-responses (up to 126 ms) recorded from extensor digitorum brevis, stimulating the deep peroneal nerve at the ankle.

The F-responses consist of Repeater F-waves. Motor conduction velocity in this condition can be very slow (e.g. 2 m/s) and in patients with clinical signs of the disease motor conduction velocity in the deep peroneal is typically less than half normal (Buchtal and Behse 1977). Lower limb nerves (and consequently muscles) are most severely affected and pathological changes are more prominant distally than proximally in the early stages (Dyck et al 1974). Kimura, using the F-response to calculate fastest motor conduction velocity over the proximal and distal nerve segments, found abnormalities of conduction compatible with the pathological findings mentioned above, i.e. in mildly affected nerves, motor conduction may be slowed in the distal segment but be in the normal range more proximally (Kimura 1974). In advanced cases F-wave transmission is slowed proximally as well as distally.

In the hypertrophic type of inherited neuropathy, F-wave analysis adds nothing useful to the information obtained from conventional motor and sensory conduction velocities when compound muscle action potentials and sensory action potential amplitudes and durations are measured. The same is true for the electrophysiological assessment of apparently unaffected relatives of affected patients.

There are no published studies (that the author is aware of) documenting F-wave latencies in Type II hereditary sensori-motor neuropathy. In some patients with this type of neuropathy motor nerve conduction can be normal in arms and legs: in the peroneal nerve, Buchtal and Behse (1977) found the slowest motor conduction velocity to be 60% of normal in their patients. F-wave latency abnormalities might, theoretically, be a sensitive index of motor fibre dysfunction, particularly in the early phase, in some patients with this type of inherited neuropathy, i.e. those with slowed motor conduction.

4.1.6. Critically ill polyneuropathy

A polyneuropathy sometimes severe and predominantly distal in distribution can complicate the course of critical illness (Bolton et al 1984). Patients who develop this type of neuropathy are sufficiently ill to require assisted ventilation. Sepsis (invariably present) and multi-organ dysfunction are complicated by muscle weakness, hyporeflexia and difficulty in weaning from artificial ventilation. The pattern of muscle weakness is, characteristically, prominent in the limbs and spares neck, tongue and jaw (Bolton et al 1986). The electrophysiological findings in these patients include reduced compound muscle and sensory nerve action potentials, prominent muscle denervation and retention of fastest transmitted sensory and motor nerve impulses: all suggestive of a primary axonal degenerative process. Post mortem studies support these findings and have failed to provide evidence of an inflammatory process of the Guillain-Barré type (Bolton et al 1986). Whether patients with this type of polyneuropathy are suffering from an illness aetiologically different from Guillain-Barré syndrome has not been fully established. Some features studied by Bolton and colleagues suggest this illness may be different from Guillain-Barré syndrome. F-wave latencies have been found to be statistically different in critically ill polyneuropathy patients and patients with Guillain-Barré syndrome, compatible with the concept that the former is a result of primary axonal degeneration while the latter is primarily a demyelinative condition.

4.1.7. Motor neurone disease

The electrodiagnostic abnormalities which can be detected throughout the evolution of this illness reflect the sequence of pathological changes in nerves and muscles. Electromyography is the examination of choice in defining the nature and extent of the process but nerve conduction studies

can be helpful through demonstrating the retention of sensory potentials, particularly when patients have subjective sensory symptoms, as is not uncommon. The results of motor conduction velocities from different studies conflict. Some workers have found slight or moderate degrees of slowing of motor conduction (Ertekin 1967, Argyropoulos et al 1978) while others have failed to replicate this and have found, instead, that fastest conducting alpha axons were not lost preferentially but were preserved for a long time in the course of the disease (Hausmanowa-Petrusewicz and Kopec 1973, Hansen and Ballantyne 1978).

If fastest conducting motor fibers were preserved one would anticipate that F-response latencies would remain within normal limits and, indeed, such a retention of fastest conducted F-waves can be found even in wasted muscle (Argyropoulos et al 1978). F-wave latency measurements, unlike EMG, are not helpful in determining the anatomical extent of motor fiber dysfunction in the early phase of the illness when diagnosis can often be difficult.

Albizzati and colleagues (1976) found that F-wave conduction velocity decreased progressively from the distal to the proximal motor segment (in the ulnar nerve) in patients with amyotrophic lateral sclerosis but, this finding has not been confirmed by other workers in lower limb nerves (Argyropoulos et al 1978).

Argyropoulos and his colleagues (1978) were interested to see if F-waves represented conduction in remaining fastest alpha axons in the presence of a depleted motor neurone population, as occurs in a process like motor neurone disease. They found that fastest conducting axons which transmitted the earliest M component also transmitted the shortest latency F-response.

In motor neurone disease some motor nerve fibres may conduct at a velocity much below that of normal slow conducting fibres resulting in an increased range of conduction velocities (Hausmanowa-Petrusewicz and Kopec 1973). Whether or not the central "turnaround" time for the F-response in the somata of the anterior horn cells is modified in motor neurone disease is unknown, but the concept is of interest (Lachman et al 1980). Even when muscular atrophy is present, earliest F-wave latencies may still be recorded in the normal range and this suggests it is less likely that the process modifies "turnaround" time in fastest conducting neurones.

Petajan (1985) believed that less variability in F-waveforms could be expected in muscles affected by neurogenic atrophy on the basis of a reduction in the number of motor neurones capable of responding to a peripheral nerve stimulus but did not provide evidence strong enough to support the hypothesis. In that study inadequate controls were included to provide appropriate comparison with muscles affected by neurogenic atrophy and the use of the deep peroneal nerve to test the prediction was inappropriate (see 2.2).

Morimoto (1980), in a very small group of patients, noted a reduction in the frequency at which F-responses could be recorded. The author's own observations on patterns of F-wave genesis in motor neurone disease are contained in 4.3

4.1.8. Radiculopathy

H-reflexes recorded from flexor carpi radialis and soleus have been found useful in the identification of root compression syndromes (Braddom and Johnson 1974, Deschuytere et al 1976). Attempts have been made to determine whether single root lesions can influence the integrity of the H-reflex of flexor carpi radialis and, in some individuals, reflex impulses

appear to be conducted along root C6, and in others along root C7 (and possibly from both, in a minority) (Schimsheimer et al 1985). Why the reflex should traverse a single spinal segment when afferent volleys are set up in at least two dorsal roots (C6 and C7), and why the segment should differ from one individual to another is puzzling (Goodgold 1974). The H-reflex is not found in other muscles of the adult hand and forearm so its diagnostic use is limited by anatomical constraints. If the F-response were to provide an alternative means of assessing conduction across specific motor roots it would be invaluable, as at the moment, clinical neurophysiological methods are particularly unrewarding in the detection of single motor root lesions.

Lesions confined to the dorsal roots do not appear to influence F-wave transmission latency and patients who have had sensory rhizotomies in cervical and lumbo-sacral territories remain capable of conducting normal latency F-responses (Magladery and McDougal 1950, Thorne 1965, Mayer and Feldman 1967, Miglietta 1973).

The F-wave has, however, proved to be of limited use in detecting and localising radicular nerve lesions. This is particularly so for single root lesions. The literature on the subject is scant and of poor quality (Eisen et al 1977(b), Fisher et al 1978(b), Tonzola et al 1980). F-wave latency measurements are of much less value, in the author's experience, than routine electromyography in the assessment of radiculopathy and there are reasons which predict this. The F-wave recorded from any skeletal muscle in the upper or lower limb is derived from spinal motor neurone pools whose axons exit through two or more root foramina (Goodgold 1974). It can be anticipated that the motor axons traversing a single undamaged ventral root unaffected by the pathology compromising the other root(s) will contain fastest conducting fibres and be capable of transmitting an F-response with a minimal latency in the normal range for the test mixed nerve/muscle. The

motor fibres which conduct F-waves with a minimal latency would have to be damaged in all roots supplying the test muscle before a pathologically prolonged minimal F-wave latency could be recorded. It is therefore surprising to find studies in which a high proportion of subjects with back pain and/or lumbosacral root compression are reported to have F-wave latency abnormalities (Eisen et al 1977(b), Fisher et al 1978(b), Tonzola et al 1980). This is particularly so when soleus F-wave latency abnormalities are not associated with soleus H-reflex latency changes (Fisher et al 1978(b)). The author's personal experience of F-wave analysis in the investigation of patients with sciatica, with or without absent ankle jerks/H-reflexes, has not been encouraging. At the present time, F-wave measurements have not been widely adopted in clinical neurophysiology laboratories for the evaluation of sciatica. The practice is, perhaps, somewhat different in the United States where referrals of sciatica from orthopaedic clinics to electrodiagnostic laboratories are commoner than in the United Kingdom. Electromyography is more likely to detect the presence of a motor fibre lesion than F-wave studies in cases of a mono-radicular lesion, but electromyography, too, can detect only a certain type of lesion (one producing denervation).

The commonest single root lesions of the upper limb affect either the C5 or the C6 roots. Recording F-waves derived through those roots in the proximal muscles of the arm is hampered by the short length of the motor axons between spinal cord and the test muscle. If a stimulus is applied at Erb's point the F-waves evoked, e.g. in infraspinatus or brachioradialis, are buried in the later components of the M wave. An alternative method for eliciting F-responses which might have an application in the study of the C5/6 motor roots will be discussed in 6.9.

The F-response can, however, be used to detect lesions within the spinal canal (intradural and extradural) which affect all roots subserving the test muscle. In patients with epidural metastatic deposits which affect both the C8 and T1 roots ulnar nerve/abductor digiti minimi F-wave latency abnormalities have been demonstrated, while distal segment motor nerve conduction velocities remain normal (Ongerboer de Visser et al 1982).

Lumbosacral root lesions which have been investigated by F-wave latency analysis (usually proximal segment F-wave conduction velocity) have, so far, been largely confined to degenerative diseases (spondylosis) and disc protrusions as far as the author can determine (Eisen et al 1977(b), Fisher et al 1978(b), Tonzola et al 1980). Lumbosacral polyradiculopathies resulting from a variety of underlying pathological mechanisms (e.g. inflammatory, traumatic and neoplastic), are less frequent clinical problems, but could be profitably studied using F-responses from appropriate calf and foot muscles. Tumours of the cauda equina are an example, although in some cauda equina lesions the presence of a multiple motor polyradiculopathy would usually be preceded by symptoms highly suggestive of a lesion in the caudal spinal canal, e.g. rectal pain and impotence in a conus lesion.

Spinal canal stenosis typically presents with exercise-related paraesthetic, numb, weak feelings in the lower limbs eased by rest and the adoption of a flexed posture (Adornato and Glasberg 1980). The transient dysfunction which may take place in the cauda equina motor fibres may be identifiable by finding reversible exercise-induced prolongation of F-response latencies in calf and/or foot muscles (unpublished observations). If this is confirmed, it may prove an important use of the F-wave in detecting a task related alteration in function of motor axons.

Studies of proximal nerve segments which identify reduced F-wave conduction velocity cannot discriminate between root and plexus involvement in conditions which may affect nerves at either site, e.g. diabetes

mellitus or Guillain-Barré syndrome (Conrad et al 1975, Panayiotopoulos 1978(a), Kimura et al 1979, Chokroverty 1980).

Ablation of F-responses can occur in motor root avulsion and traumatic brachial plexus lesions (usually in motor cycle accidents). The early differentiation of the two lesions can be difficult and is not usually aided by F-response studies. Retention of the F-response points to anatomical continuity between cord and muscle. If voluntary motor unit recruitment is retained, however impaired, lower motor neurone connectivity with muscle must be retained and the F-response can add nothing further.

The possibility of simultaneous compression of a mixed peripheral nerve and its sensory and motor fibres traversing plexus or roots was suggested by Upton and McComas (1973) and has since been documented with a surprisingly high prevalence in a group of patients with peripheral nerve entrapment syndromes (Eisen et al 1977(a)). The coexistence of an associated proximal lesion might partly explain the incomplete symptomatic response to surgical release seen in some patients treated for median nerve entrapment in the carpal tunnel. Clues to the presence of a "double crush" phenomenon can be got from F-wave studies by calculating the F ratio or F-wave conduction velocity over the proximal segment (see 2.1.4, 2.1.5) (Eisen et al 1977(a)). Precise localisation of a proximal lesion to root or plexus level in this setting is not possible using F-wave studies alone.

4.1.9. Plexopathy

Introduction

Various techniques for comparing proximal and distal segment conduction latency in the fastest conducting motor axons supplying the intrinsic hand and forearm muscles can be applied to detect brachial plexus

lesions. These include the F-ratio, the calculation of proximal segment F-wave conduction velocity and the measurement of conduction latency in the axilla-cord segment of the C8-T1 motor fibres. These techniques are detailed in Chapter 2.

Diverse lesions, be they traumatic (e.g. stab wounds), inflammatory, neoplastic, radiation-induced (Esteban 1986), or mechanical (e.g. iatrogenic, (Jackson and Keats 1965)), can result in slowing of impulses as they traverse the proximal segment of the lower motor neurones at plexus level. Reference has been made to inflammatory causes of plexopathy in more detail in 4.1.3. F-wave abnormalities relating to tumour invasion, radiation damage and mechanical damage from a cervical rib and band will be considered here.

Radiation and Tumour Related Plexopathy

Brachial plexopathy occurring in patients with neoplasia usually results from tumour infiltration or injury from radiation therapy. In patients who have had radiation therapy for neoplasia (e.g. lymphoma) F-wave latencies measured from the intrinsic muscles of the hand are most likely to be abnormal when tumour has spread to involve the brachial plexus, as direct invasion tends to involve the lower trunk while radiation-related lesions more commonly damage the upper trunk (Kori et al 1981). Many patients with metastatic brachial plexopathy also have epidural disease from tumour infiltration along the nerve roots through the intervertebral foramina (Kori et al 1981). Delayed F-waves in the intrinsic hand muscles of a patient with neoplasia could therefore arise from a lesion in the brachial plexus or one which primarily involves roots at the epidural level or a lesion which has spread from the plexus proximally through the intervertebral foramen. It is important to detect epidural extension early to plan appropriate treatment

(Gilbert et al 1978). Although C8,T1 segment F-responses are more likely to be affected by neoplastic infiltration of the plexus than by radiation damage in a person who has had radiation therapy for neoplasia, the important differentiation between a lesion confined to either the epidural roots, the lower trunk of the plexus or involvement of both, cannot be made using the F-response and additional techniques such as myelography and CT body scanning are necessary (Ongerboer de Visser et al 1982). The interpretation of F-wave latency abnormalities, as has been pointed out earlier, must be determined by associated features, be they clinical signs, other electrodiagnostic signs or the results of other types of investigations such as neuroradiological investigations. F-wave latency results have to be interpreted in the light of the patient's presentation.

Thoracic outlet syndrome

Brachial plexopathy resulting from a cervical rib or band is uncommon and confirmatory electrodiagnostic features are absent in the vast majority of patients referred to EMG laboratories with thoracic outlet syndrome as a proposed diagnosis (Shahani et al 1980(c)). The classical electrodiagnostic signs of the syndrome are a small amplitude ulnar sensory action potential and electromyographic signs of partial denervation in the C8,T1 innervated intrinsic hand muscles (Gilliatt et al 1970, Gilliatt et al 1978). In patients whose syndrome has evolved to an extent where wasting is present in the hand, thenar wasting can be more prominent than hypothenar wasting. Prolonged F-wave latencies through either, or both, the ulnar and/or the median nerve to the hypothenar and thenar muscles, respectively, have been described (Weber and Piero 1978, Dorfman 1979, Wulff and Gilliatt 1979) and are typically associated with a maximal motor nerve conduction velocity in the normal range over the forearm segment of the test nerve (Wulff and

Gilliatt 1979). Wulff and Gilliatt (1979) noted that a post-operative improvement in F-wave latency could occur after removal of an anomalous band connecting the C7 transverse process and the first rib. The finding of delayed ulnar and median nerve F-waves in a hand with thenar and/or hypothenar wasting still leaves a differential diagnosis of disparate conditions, e.g. syringomyelia (Peioglou-Harmoussi et al 1986). Associated electrodiagnostic findings may help in some instances; for example, the coexistence of a reduced ulnar sensory action potential would be in keeping with a plexus lesion rather than a preganglionic sensory lesion as might occur with syringomyelia.

4.1.10. Syringomyelia

Patients with cervico-dorsal syringomyelia are at risk of developing upper limb peripheral nerve entrapment syndromes, particularly of the ulnar nerve at the elbow (Peioglou-Harmoussi et al 1986). This complicates the study of F-wave parameters relating purely to the intraspinal lesion as delayed F-waves or excessive F chronodispersion may be the only indication of a peripheral mixed nerve lesion (Lachman et al 1980). There are a number of reasons for this predisposition to associated peripheral nerve lesions and they include coexistent disorganised joints and immobility of the limbs.

Sensory and motor nerve conduction studies of the distal portions of the ulnar and median nerves are insensitive in detecting intraspinal pathology although the retention of normal sensory action potentials in a patient with dissociated sensory loss associated with neurogenic atrophy is highly suggestive of a lesion inside the spinal cord. (Peioglou-Harmoussi et al 1986). Cord cavitation producing muscular wasting and weakness does not result in slowing of motor nerve conduction velocities until the pathological process advances to a stage where function in the largest motor neurones is

lost.

Several studies have described altered F-wave latencies in the hand and forearm muscles in association with a cervico-dorsal syrinx (Dyro et al 1983, Rossier et al 1985, Peioglou-Harmoussi et al 1986). The most convincing evidence that syringomyelia in itself modifies the responses of motor neurones to antidromic volleys comes from pre- and post-operative studies on post-traumatic syringomyelia (Rossier et al 1985). In that study F-wave latency abnormalities were, in some cases, corrected by surgical drainage of the cavity suggesting that the origin of the delayed motor conduction lay within the spinal cord. The application of F-wave conduction velocity and F-ratio techniques to "localise" the lesion(s) producing F-wave delays in syringomyelics have not been published in the literature on the subject. The pathophysiology of this reversible functional disturbance of the lower motor neurones is unclear but effects might be expected at a number of sites within the spinal cord. For example, a syrinx might have direct effects on anterior horn cells, on the intraspinal motor axons or at intraspinal inputs onto motor neurones (from the suprasegmental level and from ipsisegmental sensory and motor cells). Disrupted function at any or all of these sites might influence the numbers of functioning anterior horn cells and/or their liability to be backfired by an antidromic volley.

It might be predicted that F-wave amplitude could be altered by a lesion which produces effects on both upper and lower motor neurones and this has been reported in some cases where a tendency to increased F-wave amplitude was seen (Peioglou-Harmoussi et al 1986). These changes could result from a combination of an upper motor neurone lesion and an enlargement of motor units following reinnervation. Peioglou-Harmoussi et al (1986) noticed that variation in F-wave configuration was similar in cases associated with little wasting of the test muscle to that seen in control

subjects, but in individual test muscles which were atrophic there was a tendency for identical F-wave forms to recur. This was not, however, quantified.

The author has published some data on a small number of patients with cervico-dorsal syringomyelia describing modified patterns of F-responses which appear in ipsisegmental hand muscles (Macleod and Shahani 1987). An illustrative case report is contained in 4.5.

4.1.11. Paediatric patients

F-response recording offers some advantages in the study of peripheral motor nerve fibre function in the newborn and the child. F-waves obtained from a single stimulation site (sometimes all a child will allow) give information on conduction along the entire nerve and obviate the need of distance measurements. Calculations incorporating short distance measurements in children can introduce relatively large errors in the calculation of conduction velocity (Ackil et al 1978).

The maximal motor nerve conduction velocity in the newborn is approximately half the adult value and this results in a relatively late minimal F-wave latency for whatever test nerve/muscle in relation to the paediatric subject's height (Shahani and Sumner 1981). A multiple regression equation can be used to predict the expected F-response latencies of a test nerve/muscle according to age and height in health (Weber and Piero 1978), but few, if any, laboratories have adequate control values for paediatric subjects.

4.1.12. Acute and Chronic Suprasegmental Pyramidal Tract Lesions

Animal experiments have shown that antidromic impulses can fail to enter the somata of some motor neurones (Lloyd 1943(a), Barakan et al 1949). If a maximised antidromic volley is backfired into a spinal motor neurone pool it fails to block a reflex volley completely unless the opposed volleys clash in the motor axons (Lloyd 1943(a)). When the sensory and motor stimuli are applied so that the two volleys meet in the motor neurones at a point proximal to the axon hillock some impulses in the orthodromic volley are not extinguished by those travelling antidromically. At any given moment the majority of anterior horn cells innervating human intrinsic hand and foot muscles cannot generate an F-wave in response to an antidromic volley (Magladery and McDougal 1950, Thorne 1965, Schiller and Stålberg 1978, Eisen and Odusote 1979). The F-wave amplitude expressed as a percentage of the M amplitude in those muscles in health is less than 5% and usually approximately 1% (Fisher 1978, Eisen and Odusote 1979, Kimura et al 1984). Current evidence suggests that the F-response represents infrequent activity in all cells of the test motor neurone pool, but within the motor neurone pool of abductor digiti minimi there seems to be a differential capacity to generate F-responses in different motor neurones (Schiller and Stålberg 1978). In short duration experiments, studying F-wave genesis in single motor units, a large percentage of neurones failed to generate an F-response but all tested motor neurones of that muscle were capable of generating an F-response in the longer duration experiments (the differences between the stimulus strength used in that experiment and the supramaximal shocks, conventionally used to evoke F-waves, has been noted and discussed earlier (see 1.4.2)). Collision studies have shown that slow as well as fast conducting motor neurones are capable of participating in the surface recorded F-response (Kimura et al 1984). The experiments of Schiller and Stålberg

used submaximal stimuli which have a bias against the activation of smaller motor neurones. Kadrie and colleagues (1976) have, however, showed that the rank order of excitability of motor units to nerve stimulation does not follow the size principle (as size relates to threshold for electrical excitation) exactly. It is noteworthy that Trontelj has failed to record F-responses from single motor neurones in orbicularis oculi (Schiller and Stålberg 1978). This may be related to the smallness of those somata (Eccles 1955).

There is, at this time, no means of determining the exact number of motor units represented in a single F-response recorded with a surface electrode. The size of a surface recorded muscle action potential is related to the number of depolarised motor units in the recording volume of the electrode and this had led investigators to use the amplitude of the F-wave as a measure of motor neurone excitability (Fisher 1978, Fisher et al 1978(a), Eisen and Odusote 1979). The inaccuracies inherent in calculating the fraction of the motor neurone pool activated antidromically by dividing the M amplitude by F amplitude are considered in 2.3.4.

The potential for an objective and simply performed neurophysiological method for quantifying spasticity is obvious, particularly with a view to monitoring any evolution in an individual patient's condition, and, more importantly, the response to a treatment. Studies reported, so far, suggest that changes in F-wave amplitude and F-wave persistence appear to parallel changes in tone, power and reflexes apparent on a basic clinical examination (Fisher et al 1978(a)).

If the effect of an acute suprasegmental pyramidal tract lesion on the motor neurone pool of abductor pollicis brevis is followed in time, changes in F-wave amplitude and F-wave persistence may be seen to evolve (Fisher et al 1978(a)). Within four weeks of an acute lesion (e.g. a cerebral infarct producing hemiparesis), F-wave impersistence and a reduction in F-wave

amplitude may be observed on the paretic side. The most prominent changes were observed in patients with the most extensive suprasegmental lesions. At this stage of the illness, the test limbs were flaccid and hyporeflexic. The changes in F-wave discharge patterns were interpreted as reflecting a reduction in motor neurone excitability to the antidromic stimuli. With recovery F-wave parameters may return to normal (Fisher et al 1978(a)).

Difficulties arise in the interpretation of results from experiments of Fisher and his colleagues due to the type of patients used to study F-wave responsiveness. Ideally, a discrete lesion localised to the suprasegmental pyramidal tract would have been most relevant. Small numbers of such patients with pure motor stroke were included but, unfortunately, no proof was offered that the patients had lacunar infarcts occurring in isolation. The majority of cases with a pure motor stroke did have an acute reduction in motor neurone excitability of abductor pollicis brevis (measured by F-wave persistence and amplitude). The patients with the greatest reduction in C8,T1 segmental motor neurone excitability had, however, signs of extensive supratentorial cerebral infarctions with signs such as dysphasia, homonymous hemianopia, cortical sensory loss and apractagnosia. The influence of suprasegmental lesions outside the pyramidal tracts on these measures of motor neurone excitability may or may not be relevant to some of those findings.

Eisen and Odusote (1979) observed that the F-wave is "easier" to elicit in muscles from a spastic limb and went on to measure maximal F-wave amplitude and mean F-wave amplitude from abductor hallucis in a group of healthy volunteers and a group of ambulant patients with lower limb spasticity. In the healthy population, the largest F-wave amplitude (peak to peak) expressed as a percentage of the M wave's amplitude was 4.5% and the average F-wave amplitude was 1% of the M wave's amplitude. They found

that in spastic legs the maximal F-wave amplitude did not increase but the average F-wave amplitude did. This suggests that a larger percentage of motor neurones than normal or a different population of motor neurones (with bigger unit territories) was activated antidromically by consecutive stimuli in the spastic limbs. The majority of patients in Eisen and Odusote's study had multiple sclerosis and the authors provide no documentation to illustrate which central nervous system tracts or structures (in addition to the pyramidal tracts) may, or may not, have been damaged by the disease process. It would, for example, be important to know whether ventral horns housing the motor neurones of abductor hallucis were damaged as can occur in some cases of multiple sclerosis. Variables, such as skinfold thickness and skin impedence, were not addressed in the papers which have considered the F-wave as a means of monitoring motor neurone excitability.

Typically, in the presence of an acute contralateral upper motor neurone lesion C8,T1 segmental motor neurone excitability is reduced in terms of F-wave persistence and amplitude, the two running in parallel (Fisher et al 1978(a)). In a small number of cases, the effects of an acute upper motor neurone lesion on F-wave persistence and amplitude were dissociated, with a reduction in F-wave amplitude found in some instances, while F-wave persistence was maintained. The opposite combination was not identified. This suggests that the effect of the pyramidal tract lesion may spare a subpopulation of anterior horn cells which are able to maintain measured F-wave persistence in the normal range.

In spastic hands, single motor unit studies using trains of stimuli, have shown that, as in normal subjects, the occurrence of F-responses is uneven (Schiller and Stålberg 1978). Of interest, the number of motor neurones failing to generate F-responses was not statistically different from the healthy state, but the F-wave persistence of responding neurones was

increased in the spastic state. In health the average F-wave persistence value in the single motor neurones of abductor digiti minimi was found to be 1 F-wave per 118 M waves, while in spastic muscle the ratio was 1 F-wave per 20 M waves. Notably, on the non-spastic side of patients with unilateral spasticity, F-wave persistence was also modified. It would appear, that in the chronic spastic state, F-wave production is facilitated in a fraction of the motor neurone pool. Slight contraction of abductor digiti minimi muscle in a spastic hand (or the contralateral healthy hand) appears capable of reducing F-wave persistence in its single motor units which display a high level of F-wave persistence in the resting state. This finding has been interpreted as reflecting blockage of soma-dendritic spikes occurring too early for orthodromic conduction (Schiller and Stålberg 1978).

4.2. Experimental Applications of the F-wave

4.2.1. Monitoring motor neurone excitability

An appropriately timed conditioning stimulus modifies the liability of a motor neurone pool to issue an F-response (Thorne 1965, Mayer and Feldman 1967, Fra and Brignolio 1968) Through quantification of the effects of conditioning stimuli on the persistence and amplitude of the F-response some measure of the excitability of a skeletal muscle's motor neurone pool might, theoretically, be obtained. Some limitations to this use of the F-response are immediately obvious. The fraction of a motor neurone pool (number and characteristics of cells) which contributes to the F-responses evoked by a series of stimuli to a mixed peripheral nerve is uncertain and variable. During a train of 100 stimuli the fraction of the whole motor neurone pool which issues an F-response will be small, just as the fraction of the motor neurone pool contributing to an individual F-wave is small (Schiller and Stålberg 1978). If, as in the cat, the somata of certain motor neurones cannot be invaded antidromically the technique could assess the properties of only a fraction of the whole pool (Renshaw 1941, Lloyd 1943(a), Barakan et al 1949, Eccles 1955). Additionally the "turnaround" time for F-responses in some smaller motor neurones is likely to be too brief to allow distal propagation as blocking of too early a soma-dendritic spike may occur at the axonal hillock.

Another major consideration is the mutability of the fraction of the test motor neurone pool capable of generating F-responses. Manoeuvres which modify the membrane potentials of motor neurones may change the population of alpha cells capable of generating F-responses. Schiller and Stålberg (1978) found that in the spastic state the high level of F-wave persistence seen in some single motor neurones could be reduced by

activation (voluntary contraction) of the test muscle or the equivalent contralateral muscle. Similarly, in health, procedures which alter motor neurone excitability could, for example, modify F-wave persistence in single motor units, by modifying the soma-dendritic membrane potential such that the orthodromic propagation of the antidromically activated anterior horn cell discharge is blocked.

Because of the variations in configurations and amplitude normally seen in consecutive F-responses evoked under stable conditions of stimulation and recording, large numbers of responses need to be averaged to obtain quantifiable data (Thorne 1965). A recovery curve for F-response numbers and amplitudes can be constructed when conditioning stimuli are delivered between 1 and 400 ms before the test stimulus (Mastaglia and Carroll 1985). With supramaximal stimuli, the recovery curve for the F-response bears some likeness to that of the H-reflex (McLeod 1969). The observed depression of the test response in the first 5 ms and then between 15 and 80 ms following the conditioning stimulus may be related to a variety of factors (Mastaglia and Carroll 1985). With inter-stimulus intervals up to Ca. 35 ms, collisions can be expected between the ascending antidromic test volley and the F-response backfired by the conditioning volley. The combined depressive effects of recurrent inhibition by the conditioning antidromic volley and presynaptic inhibition of IA afferents could be relevant to the observed depression of the test response lasting up to 80 ms (Veale and Rees 1973). In the experiments of Mastaglia and Carroll (1985) it appears there may be a sex difference in the recovery curve of the F-response. In the male, the period of depression of the test stimulus extended up to 80 ms, beyond the 35 ms seen in the females. Two-thirds of the subjects (of both sexes) showed a period of facilitation from 80 ms to 300 ms during which test F-response numbers were greater than those

recorded from a single stimulus sequence. It should, however, be noted that the number of male and female subjects studied is extremely small and does not justify a firm conclusion.

As a means of measuring motor neurone excitability, this technique has not, so far, been developed and the technical difficulties and potential drawbacks as illustrated are considerable.

High dose Thyrotropin Releasing Hormone (TRH) may, at least in the short term, improve motor strength and lessen spasticity in patients with amyotrophic lateral sclerosis (Engel et al 1983). The mechanism may, presumably, be connected with facilitation of alpha motor neurone firing. Measurement of amplitude and persistence of F-responses has been used in an attempt to study the excitability of the lower motor neurone in response to intravenous and subcutaneous TRH (Beydoun and Engel 1985). The authors reported an excitatory effect of TRH on the lower motor neurone, as gauged by the F-wave parameters they analysed. This study marks a new application in the F-response. There are difficulties in interpreting the results of this study and its reproducibility is uncertain.

Muscle spindles are highly sensitive to vibration (Hagbarth and Eklund 1966, Lance et al 1968) and, when applied to an isolated muscle, vibration has complex central effects (Magherini et al 1972, Scheippati 1987). The observation of a suppression of phasic stretch reflexes in a muscle by vibration of that muscle has been important in allowing further development in the understanding of spinal physiology (Lance et al 1966). The theory that presynaptic inhibition was the principal physiological mechanism involved in the suppression of the H-reflex by vibration followed from Lance's work which showed the afferent "busy line" theory to be inadequate as an explanation of the phenomenon (Lance et al 1968). Some support for the concept that presynaptic inhibition was a major mechanism for suppression of

the stretch reflex by vibration came from animal experiments, in which the F-response was used to test the effects of vibration on motor neurone excitability (Gillies et al 1969). In those experiments vibratory stimuli were not seen to influence the F-response at a time when there was profound suppression of the monosynaptic reflex in the same motor neurone pool. Following from this work, the effect of vibration on the monosynaptic reflex has been used (inappropriately) as a model to study presynaptic inhibition in isolation (Ashby and White 1973).

It has been shown in man, some years after the animal experiments of Gillies and colleagues (1969), that vibration does have an effect on the responsiveness of a motor neurone pool to antidromic motor volleys (Shahani and Young 1976). Both during, and after, a period of vibratory stimulation marked changes in F-wave persistence and amplitude have been seen to occur. In some test subjects both were reduced during vibration and in one subject they were increased. Post vibratory facilitation of the F-response was a consistent finding in all experiments. It is not surprising, in view of the range of peripheral receptors stimulated by vibration applied to a muscle (joint, cutaneous and muscle receptors), that post-synaptic effects on interneurones and the motor neurone pool should occur. Although the effects of vibration on the human F-response have not been studied systematically (only a very small number of subjects have been studied) the findings of Shahani and Young indicate that the interaction of vibration with the monosynaptic reflex is an inappropriate model for the study of pure presynaptic inhibition.

4.2.2. The origins of fasciculations

Denny-Brown (1949) suggested that fasciculations resulted from a "disorder of the whole excitable membrane". Recent work on the origins of fasciculations provides evidence to the contrary. A fasciculation arising from an axon may be followed by its own F-response. The time interval between these two potentials recorded from a muscle represents the time the antidromic impulse takes to travel to the anterior horn cell and back to the trigger point, and has been used to localise the origin of the faciculation along the axon (Roth 1984).

In both healthy subjects and patients who fasciculate from a variety of neurological disorders (e.g. chronic poliomyelitis, amyotrophic lateral sclerosis, polyneuropathy and plexopathy) the findings support the concept that the great majority of fasciculations have an axonal origin.

4.2.3. The investigation of central nervous system pathways

4.2.3.1. Introduction

The F-wave provides a means of determining spinal cord to muscle motor fibre transit time in different motor neurones and this in turn permits the calculation of latencies for central impulse transmission in a variety of reflex and other artefactual electrophysiological responses. The drawbacks inherent in these uses of the F-wave will be mentioned. The technique of Berger and Shahani for calculating spinal cord motor conduction latency, using the F-response, has been incorporated in this section as an experimental tool rather than in the section devoted to the electrodiagnostic use of the F-wave, as the interpretation of the results from the technique is assumptive (Berger and Shahani 1986). It may however be a very useful

method which could find a place in routine clinical neurophysiological work.

4.2.3.2. Motor conduction within the spinal cord

Stimulation of the spinal cord using a monopolar needle electrode inserted into the C5 paraspinal muscle evokes a compound muscle action potential in the tibialis anterior muscle (Berger and Shahani 1986). The assumption has been made that this response results from transmission, commencing at the mid cervical level, in the ipsilateral pyramidal tract to the motor neurone pool of tibialis anterior where a number of motor neurones are depolarised. This motor response has been used to estimate spinal motor conduction time (Berger and Shahani 1986). The latency of the response in tibialis anterior is taken to represent a central and a peripheral conduction latency. By subtracting the peripheral conduction time (from spinal cord to muscle) from the total latency, the central latency is, theoretically, obtained. The tibialis anterior F-wave latency is used to calculate peripheral conduction latency using the formula F + M -1 / 2 (ms). (F = the minimal F-wave latency, while M = the minimum M latency, both recorded from tibialis anterior stimulating the peroneal nerve the the fibular head, 1 = 1 ms "turnaround" time for the F-response) (see 2.1 where criticism of this type of calculation is contained). These workers have been tempted to correlate the central conduction latency with the spinal cord length in individual subjects, but the conversion of primary data of this type is prone to error. They have calculated "velocity indexes" by measuring the distance from C5 to the L4 spinous processes and dividing that by the central motor latency. The resultant "index" is claimed to provide an approximation of the pyramidal tract conduction velocity. Patients with multiple sclerosis (clinical features not detailed) and cervical myelopathy have been found to have

reduced "velocity indexes" below the lower limit (54 m/s) of a control range. One case of myelopathy in the study showed a reduction in spinal motor conduction latency, from above to within the control range, after surgical decompression of the cervical cord. This technique has the advantage that it is simple to perform and requires only standard equipment available in any up to date EMG labortory.

Dorfman (1977) introduced an indirect method of non-invasibly measuring spinal cord conduction velocity using the F-wave and the somatosensory evoked potential. The method involves measurement and/or the derivation of seven independent variables which results in a sizeable standard deviation for the spinal cord conduction velocity. Despite this, claims have been made that the method is of clinical use (Eisen and Nudelman 1979).

4.2.3.3. The cutaneous reflexes

Electrical stimulation of cutaneous afferents in the limb extremities can be used to evoke reflex modulations of ongoing electrical activity in a muscle during a steady voluntary contraction (Caccia et al 1973). These responses have been termed "cutaneous reflexes". The F-response has been used in the estimation of central latencies for the components of the cutaneous reflex (Jenner and Stephens 1982). The efferent conduction latency for the initial component of the triphasic response obtained from the first dorsal interosseous has been calculated using the earliest F-response latency. The residual central latency suggests that the initial component traverses a central pathway confined to the spinal cord. The inaccuracies inherent in using the F-wave latency to calculate a cord to muscle conduction latency are discussed in Chapter 2.1. In this instance, no information is available on the type of motor neurones which are reflexly

activated through the suprasegmental relay in the cutaneous reflex and so the minimal F-wave latency (which provides information on large motor neurones) (Kimura et al 1984, Shahani et al 1987) could prove to be an inappropriate measurement of motor conduction latency for the efferent limb of the reflex. By calculating the lower motor neurone transit time, using the F-response from the test muscle, inferential data on the conduction latency of the transcortical pathway of the cutaneous reflexes can also be obtained (Jenner and Stephens 1982).

4.3. The Effects of Peripheral Nerve Disorders on F-wave Persistence and Repeater F-wave Measurements: An Experiment

4.3.1. Introduction

Only a small fraction of a test motor neurone pool issues an F-wave in response to an antidromic volley (Magladery and McDougal 1950, Thorne 1965, Schiller and Stålberg 1978), Eisen and Odusote 1979, Kimura et al 1984). This phenomenon has been observed in all skeletal muscles from which F-responses have been recorded. The differences in F-wave persistence and Repeater F-wave counts in the healthy ulnar, median and peroneal nerves described in 2.2, suggest the presence of factors which determine characteristic patterns of recurrent motor dicharging from each of those anterior horn cell populations.

Diseases of the peripheral nervous system could, theoretically, lead to altered patterns of F-wave production. A number of different mechanisms suggest themselves. For example, a reduction in the number of functioning anterior horn cells or a blockade of antidromic impulse transmission in a proportion of alpha axons could result in abolition of F-responses in a fraction of the test motor neurone pool. Alternatively, centrifugal propagation of the F-response could be impeded by a distal nerve lesion when a more proximal stimulus activates an intact test motor neurone pool in the normal way. Additionally, segmental demyelination could slow motor conduction in large diameter fibres and alter the temporal profile of the antidromic motor volley, which might, in turn, influence Renshaw cell inhibitory effects and therefore the liability of individual alpha cells or groups of alpha cells to issue an F-response. As well as lesions of the motor cells and their fibres, lesions of afferent fibres in the test mixed nerve could have effects on the excitability of anterior horn cell membranes and

influence the response of those cells to the test antidromic stimuli.

There are, therefore, reasons to suggest that peripheral nervous system lesions which result in denervation, conduction block or slowed nerve impulse transmission (in either or both afferent and/or efferent fibres in the test mixed peripheral nerve) could modify the physiological patterns of F-responses normally recorded from skeletal muscle.

To determine if lesions of the peripheral nervous system influence patterns of F-wave production in the intrinsic hand muscles, 3 measurements, which quantify F-wave production (F-wave persistence, the Repeater F-wave count and the %Repeater F-wave value), have been made from the intrinsic hand muscles of a group of patients with peripheral nervous system lesions and these values have been compared with those from age-matched control subjects.

4.3.2. Methods and materials

The ulnar nerve/abductor digiti minimi and median nerve/abductor pollicis brevis were studied in a variety of disorders with embrace a spectrum of pathophysiological mechanisms and include neuronopathy, compression neuropathy, demyelinating neuropathy and metabolic neuropathy. A heterogeneous group was chosen as theoretical considerations suggested that these disparate lesions could each modify F-discharge behaviour.

The results from the control group have been reported already in 2.2 and 2.3.

F-waves were recorded from the pathological material with the same techniques which were employed in the control subjects. The methodology is described in 2.2.2 and will not be repeated here. The replication of methodology included types of electrodes, placement of electrodes, temperature control and recording conditions; wherein the patients were

supine and relaxed. The stimulus duration necessary to maximise the M wave were greater in some cases and the duration of the pulse was increased as was found necessary. The methods for calculating F-wave persistence values, Repeater F-wave counts and %Repeater F-wave values are described in 2.2 and 2.3. (see pages 68, 69, 92 and 93).

As some age-related differences in F-wave production have been identified in healthy volunteers (see Chapter 2.4) and because of differences between the F-wave generating behaviour in the different motor neurone pools of different mixed peripheral nerves (see 2.2 and 2.3) the analysis was applied to groups of age-matched ulnar and median nerves separately. It was decided to exclude subjects under the age of 26 and over the age of 65 from the study (see 2.4).

Control subjects -

One hundred and fifty-three ulnar nerves from 109 healthy volunteers, 54 male, 55 female, aged 26-65 years (mean 43, S.D. 9.5), and 147 median nerves from 99 healthy volunteers, 53 female, 46 male, aged 26-65 years (mean 43, S.D. 9.8) provided control data. The inclusion criteria for this group of nerves has already been described in 2.2.2. (page 70) and will not be reiterated. The F-response patterns generated by these nerves/muscles have already been analysed for the purpose of a comparison of F-wave production in different motor neurone pools in health (see 2.2.3).

The source of these volunteers is also described in 2.2.2.

Neuropathy subjects - Sixty-four patients, 29 males, 35 females, aged 26 to 65 (mean 46, S.D. 10.2) were studied. The types of neuropathy and the numbers of nerves studied are contained in Table 17.

TABLE 17

TYPES OF NEUROPATHIC DISORDERS IN PATIENTS WHOSE ULNAR AND MEDIAN NERVE F-WAVE DISCHARGE PATTERNS WERE QUANTIFIED

Neuropathy Type	No. of Patients	No. of Ulnar Nerves	No. of Median Nerves	Total No. Nerves
Guillain-Barré Syndrome	13	19	16	35
Motor Neurone Disease	11	10	15	25
Cubital Tunnel Syndrome	24	24	0	24
Charcot-Marie-Tooth Syndrome	6	6	8	14
Diabetic Neuropathy	6	6	7	13
Alcoholic Neuropathy	4	0	8	8
Total	64	65	54	119

In total, 119 nerves were studied, 65 ulnar and 54 median. The patients were either attending the neurophysiology laboratory at Dundee Royal Infirmary, having been referred for evaluation from the hospital's clinics or wards (mainly neurological or orthopaedic), or came from the orthopaedic department at Bridge of Earn Hospital, or were traced using the department's diagnostic register and asked to volunteer for the study. Patients with each type of neuropathy were consecutive cases of that type, aged from 26-65 years, inclusively, which met the inclusion criteria (see below).

In patients with motor neurone disease, ulnar and median nerves were included in the study only if there were clinical signs of a lower motor neurone lesion within the motor territory of that mixed peripheral nerve (wasting, weakness, fasciculation) and/or EMG signs of a lower motor neurone lesion in the test muscle. Similarly, in the cases of Guillain-Barré syndrome there were signs of lower motor neurone dysfunction within the relevant nerve territory. The diagnosis of Guillain-Barré syndrome was reached by considering the clinical presentation, CSF analysis and conventional nerve

conduction studies in conjunction. Patients with the cubital tunnel syndrome had ulnar nerve territory symptoms and signs and had electrodiagnostic verification of the lesion by conventional nerve conduction studies and electromyography. Some, but not all, patients with Charcot-Marie-Tooth syndrome, alcoholic and diabetic neuropathy had clinical signs of neuropathy in the upper limbs but all had electrophysiological evidence of nerve dysfunction in the lower limb. Four of the subjects with Charcot-Marie-Tooth syndrome were identified as type I hereditary sensori-motor neuropathy and 2 had type II patterns of abnormality on nerve conduction studies/EMG.

100 supramaximal electrical stimuli were applied to the mixed peripheral nerve of each test muscle and 100 F-wave sweeps were photographed from the oscilliscope of the electromyograph. From these photographic records 3 measurements were made for each test nerve/muscle.

1) The F-wave persistence value
2) The Repeater F-wave count
3) The %Repeater F-wave value

4.3.3. Results

F-wave persistence values, Repeater F-wave counts and %Repeater F-wave value from the group of damaged nerves are listed in Tables 18 and 19 on pages 188-191. Control values are listed on pages 74 to 80. The results are illustrated in the form of bar histograms in Figure 17, page 192.

As the data was skewed, statistical analysis on the 3 measurements for the ulnar and median nerve groups was done using a non-parametric method, the Mann-Whitney test.

TABLE 18

PERIPHERAL NEUROPATHIES
(n = 54)

MEDIAN NERVE/ABDUCTOR POLLICIS BREVIS

Nerve No.	F-wave Persistence	Repeater F-wave Count	%Repeater F-wave value	Diagnosis
1.	28	23	82	MND
2.	70	50	71	"
3.	100	100	100	MND
4.	100	100	100	"
5.	67	55	82	MND
6.	100	100	100	GBS
7.	82	77	94	"
8.	10	10	100	GBS
9.	20	16	80	"
10.	42	42	100	GBS
11.	39	30	77	"
12.	54	42	78	GBS
13.	72	56	78	"
14.	15	10	67	GBS
15.	58	43	74	"
16.	6	4	67	GBS
17.	56	53	95	"
18.	45	23	51	GBS
19.	5	5	100	MND
20.	3	3	100	"
21.	55	33	60	MND
22.	100	100	100	MND
23.	100	100	100	"
24.	100	100	100	MND
25.	61	18	30	"
26.	90	11	12	CMT
27.	71	28	39	"
28.	87	48	55	CMT
29.	32	21	66	"
30.	95	6	6	CMT
31.	92	27	29	"
32.	74	18	24	CMT
33.	58	31	53	"
34.	51	8	16	DM
35.	47	10	21	"
36.	95	2	2	DM
37.	81	31	38	"
38.	32	27	84	DM
39.	18	16	89	"
40.	52	9	17	DM
41.	17	17	100	MND
42.	43	42	98	"
43.	82	70	85	MND
44.	35	9	26	GBS

Nerve No.	F-wave Persistence	Repeater F-wave Count	%Repeater F-wave value	Diagnosis
45.	48	30	63	GBS
46.	30	25	83	GBS
47.	80	18	23	APN
48.	72	31	43	"
49.	98	14	14	APN
50.	92	11	12	"
51.	51	29	57	APN
52.	88	34	39	"
53.	90	4	4	APN
54.	86	17	20	"

Key:

GBS	- Guillain-Barré syndrome
MND	- Motor neurone disease
CUB	- Cubital tunnel syndrome
CMT	- Charcot-Marie-Tooth syndrome
DM	- Diabetic neuropathy
APN	- Alcoholic peripheral neuropathy

TABLE 19

PERIPHERAL NEUROPATHIES
(n = 65)

ULNAR NERVE/ABDUCTOR DIGITI MINIMI

Nerve No.	F-wave persistence	Repeater F-wave count	%Repeater F-wave value	Diagnosis
1.	52	46	88	MND
2.	25	25	100	GBS
3.	62	60	97	GBS
4.	12	9	75	MND
5.	28	23	82	MND
6.	40	32	80	MND
7.	70	50	71	MND
8.	55	40	73	GBS
9.	58	17	29	GBS
10.	62	15	24	CUB
11.	78	9	12	CUB
12.	70	36	51	CUB
13.	70	70	100	MND
14.	82	57	70	MND
15.	42	36	86	GBS
16.	75	45	60	GBS
17.	80	47	59	CUB
18.	28	15	54	CUB
19.	80	15	19	CUB
20.	75	70	93	GBS
21.	100	100	100	GBS
22.	75	33	44	DM
23.	60	47	78	DM
24.	72	13	18	DM
25.	60	12	20	DM
26.	95	15	16	CUB
27.	78	14	18	CUB
28.	70	7	10	CUB
29.	90	12	13	DM
30.	80	32	40	DM
31.	39	30	77	MND
32.	75	72	96	MND
33.	99	56	57	GBS
34.	87	30	35	GBS
35.	68	44	65	GBS
36.	83	27	33	CMT
37.	51	47	92	CMT
38.	84	37	44	CMT
39.	10	10	100	MND
40.	72	40	56	GBS
41.	100	33	33	GBS
42.	66	40	61	GBS

Nerve No.	F-wave persistence	Repeater F-wave count	%Repeater F-wave value	Diagnosis
43.	75	20	27	GBS
44.	52	20	38	CUB
45.	42	36	86	CUB
46.	54	45	83	CUB
47.	80	80	100	CUB
48.	100	100	100	CUB
49.	60	15	25	CUB
50.	59	10	17	CUB
51.	66	8	11	CUB
52.	74	19	26	CUB
53.	58	10	17	CUB
54.	72	6	8	CUB
55.	26	12	46	CUB
56.	59	15	25	CUB
57.	68	50	74	CUB
58.	78	12	15	CUB
59.	90	30	33	CMT
60.	95	9	9	CMT
61.	66	20	30	CMT
62.	44	32	73	GBS
63.	40	30	75	GBS
64.	100	80	80	GBS
65.	18	15	83	GBS

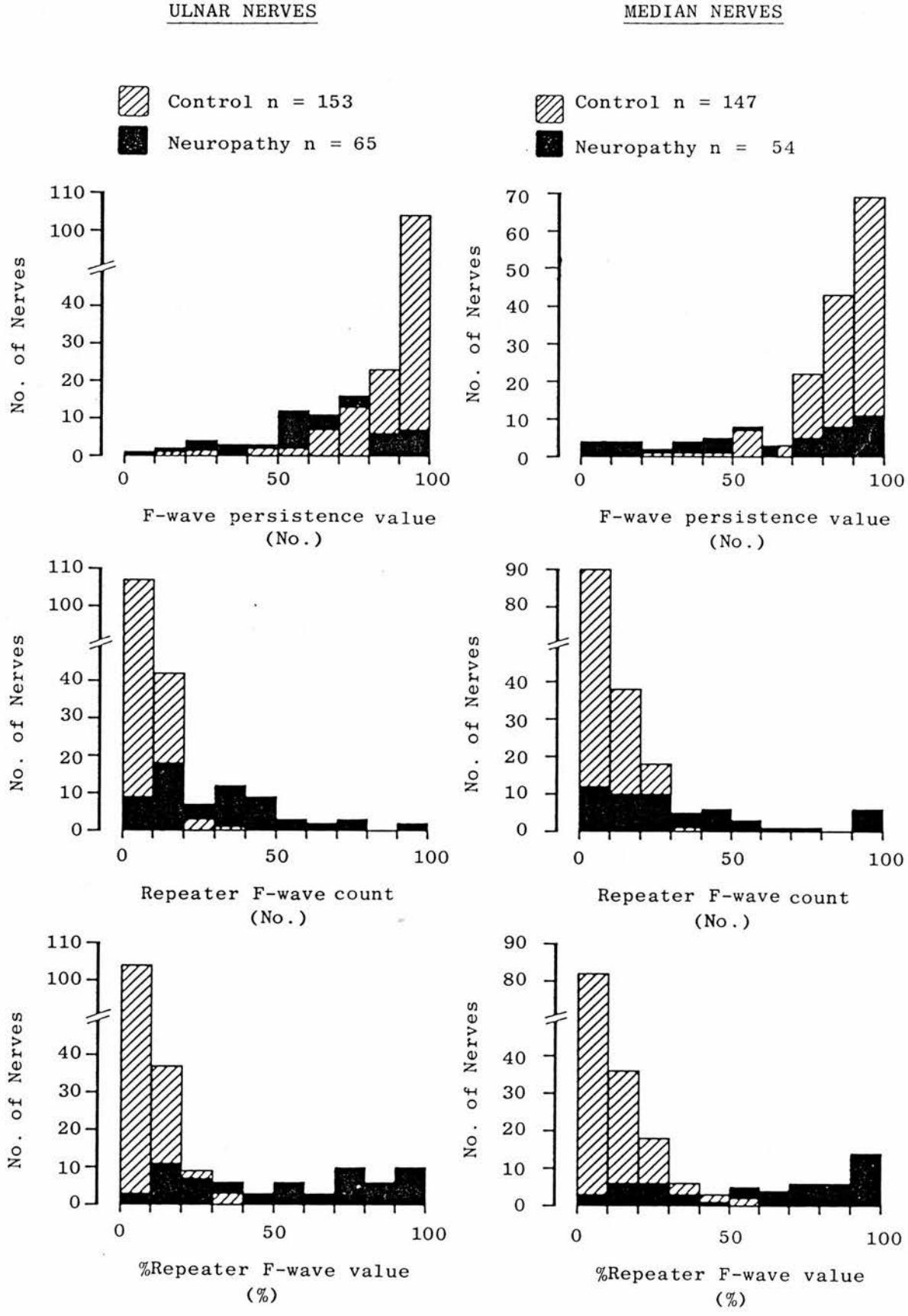


FIGURE 17

F-wave persistence, Repeater F-wave values and %Repeater F-wave values in age-matched healthy volunteers and patients with "neuropathy".

F-wave persistence - There was strong evidence that F-wave persistence has been altered by the presence of peripheral nerve dysfunction in both the ulnar and median nerve groups ($p<0.0001$). In the control median nerve group 76% of values lay above 80, while in the neuropathy group the figure was only 35%. Associated with this drop in F-wave persistence for the group as a whole, the lower end of the range fell from 25 in the control group to 3 in the median neuropathy group. Fifteen percent of damaged median nerves had values below the lower limit of the control range. It would seem, therefore, that a large number of test median nerves had F-wave persistence values which remained within the range found in the healthy state, while as a group there was a significant drop in F-wave persistence. The same pattern was observed in the group of damaged ulnar nerves.

Repeater F-wave count - The number of Repeater F-waves recorded from the median neuropathy group was significantly higher ($p<0.0001$) than in the control group. Thirty-one per cent of median nerves in the neuropathy group had values above the highest value, 35, recorded from an individual healthy median nerve.

In the ulnar nerves analysed, there was also strong evidence of a difference between the control and neuropathy groups ($p<0.0001$), the latter generating more Repeater F-waves. Forty-three per cent of the nerves from the ulnar neuropathy group had Repeater F-wave values greater than the highest value, 32, seen in an individual healthy ulnar nerve.

The two neuropathy groups discharged fewer F-responses than their age-matched control groups and those responses were comprised of less variable waveforms. These two differences are exemplified in Figure 18 by a damaged nerve which discharged only 11 F-responses (reduced F-wave persistence) to 100 stimuli, all of which were Repeater F-waves (see [A]).

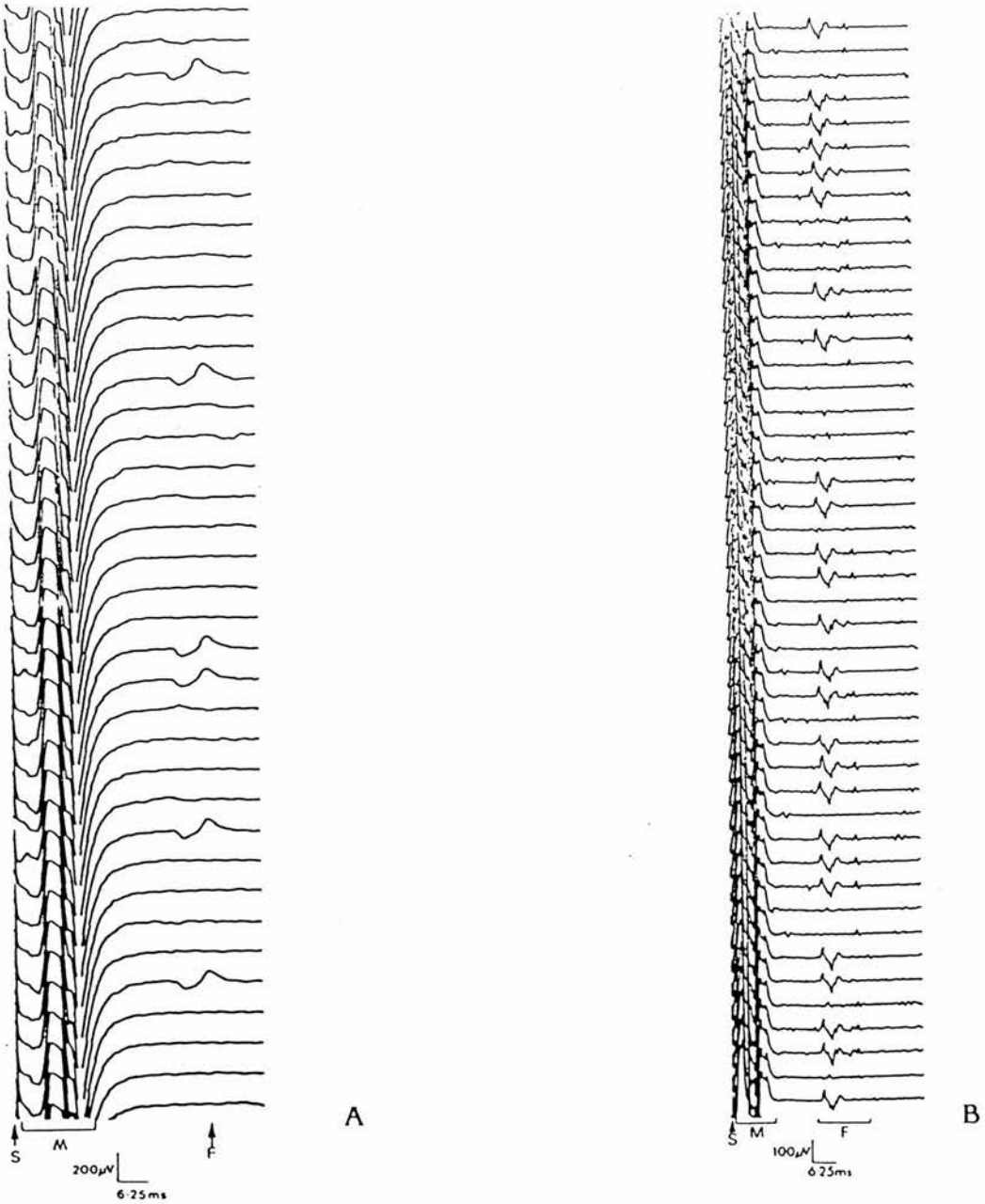


FIGURE 18

DIFFERENT PATTERNS OF PERSISTENCE OF REPEATER F-WAVES

A: Recorded from the motor point of abductor pollicis brevis of a patient with Guillain-Barré syndrome (acute phase). The F-wave persistence value was 11 (from 100 stimuli). An individual Repeater F-wave is the only F-response.

B: Recorded from the motor point of abductor pollicis brevis from a different patient with acute Guillain-Barré syndrome (acute phase). F-persistence value was 74 (from 100 stimuli) (only the initial F-response in a sweep included in the analysis). There is reduction in the usual variability of F-waveform but the persistence value is within the 'normal' range.

In both muscles Repeater F-waves are present in A, 1 type of Repeater F-wave, and in B, several types of Repeater F-waves).

In some damaged nerves/muscles, however, while F-waveforms were less variable they could appear, not impersistently, as predicted, but at a pathologically high level of persistence. The second example in Figure 18, [B], illustrates this pattern of F-wave discharges. A single individual Repeater F-wave is generated by the majority of stimuli, while activity in the remainder of the test motor neurone pool is "suppressed". Note that each sweep may contain more than 1 F-response; (see below).

%Repeater F-Wave Value - A reduction in F-wave persistence and a contraction of the fraction of the alpha motor neurone pool active in generating F-responses are both reflected in the %Repeater F-wave values obtained from median and ulnar neuropathy groups. There is strong evidence that the %Repeater F-wave value of the control and neuropathy groups are different ($p<0.0001$) in both ulnar and median nerve groups.

The median nerve control range was 0% to 60%. Ninety-two per cent of control %Repeater F-wave values were $\leq$30%, while 72% of the median neuropathy %Repeater F-wave values were >30%. %Repeater F-wave values up to 100% were recorded in the neuropathy group.

The ulnar nerve control range extended from 0-33%. Ninety-two per cent of healthy control nerves had %Repeater F-wave values $\leq$20% and in the neuropathy group 63% of nerves had %Repeater F-wave values above the upper value of the control range.

%Repeater F-wave values above the control range upper limit were seen in all types of neuropathy included in the study. The upper range %Repeater F-wave values of individual nerves from both groups of healthy nerves were made up of multiple Repeater F-wave types (usually less than 10), i.e. each Repeater F-wave seen in a control group appeared at a low level of persistence. In the neuropathy groups small numbers of Repeater

F-wave types, e.g. one or two, often comprised a high %Repeater F-wave value (see Figure 18). If the persistence level was low only small numbers of Repeater F-waves need appear to produce a high %Repeater F-wave value and this was the anticipated pattern of abnormality. Highly persistent individual Repeater F-waves (Figure 18 [B]) were not anticipated. Some damaged nerves generated multiple Repeater F-waves which were persistent; sometimes each sweep contained only 1 F-wave while others contained a sequence of Repeater F-waves. These pathologically persistent Repeater F-responses appeared either in the "normal" latency range (typically in motor neurone disease; see Figure 19), or beyond it. Figure 20 shows pathological F chronodispersion of 2 individual Repeater F-waves, one appearing persistently, the other (later one) impersistently. Such delayed Repeater F-waves were characteristic of deymelinating neuropathies such as Charcot-Marie-Tooth disease (see Figure 16) and Guillain-Barré syndrome.

It was common for a damaged nerve to produce not one, but two, or more, individual Repeater F-waves in response to a single stimulus. These backfired responses appeared "in series" i.e. more than one F-wave appeared in a sweep (Figure 21). No count was made of the Repeater F-wave responses "in series" in the control group versus the neuropathy group but it was clear they were very uncommon in healthy nerves.

Some damaged nerves generated very complex patterns of F-responses "in series". Figure 22 shows the F-responses recorded from abductor pollicis brevis in a patient with acute phase Guillain-Barré syndrome. F-wave no. 2 appears in every sweep (except those which contain F-wave no. 1). Other Repeater F-waves occur at different levels of persistence and in varying combinations.

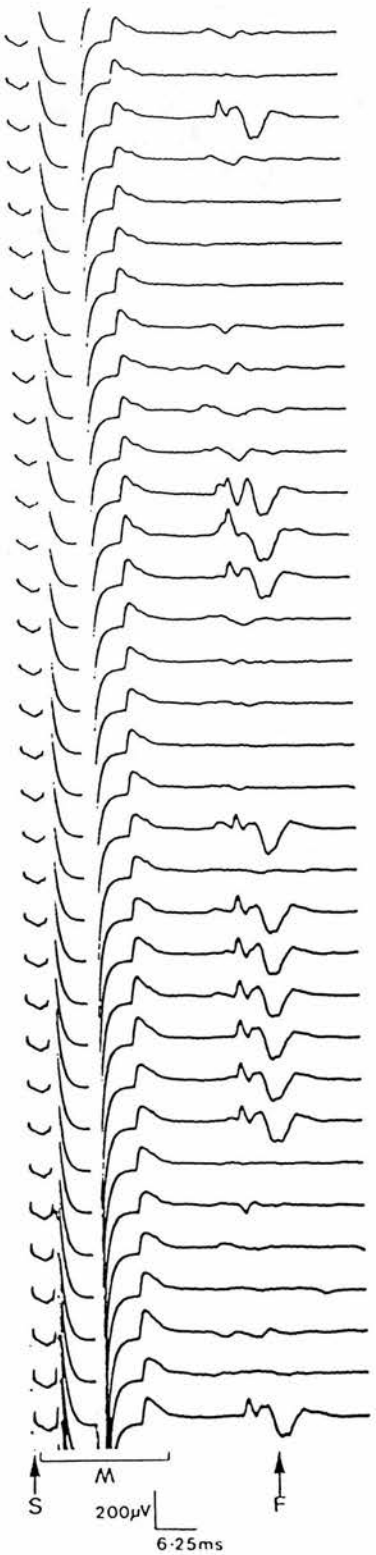


FIGURE 19

NORMAL LATENCY HIGHLY PERSISTENT INDIVIDUAL REPEATER F-WAVE

Recorded from the wasted abductor pollicis brevis of a patient with motor neurone disease.

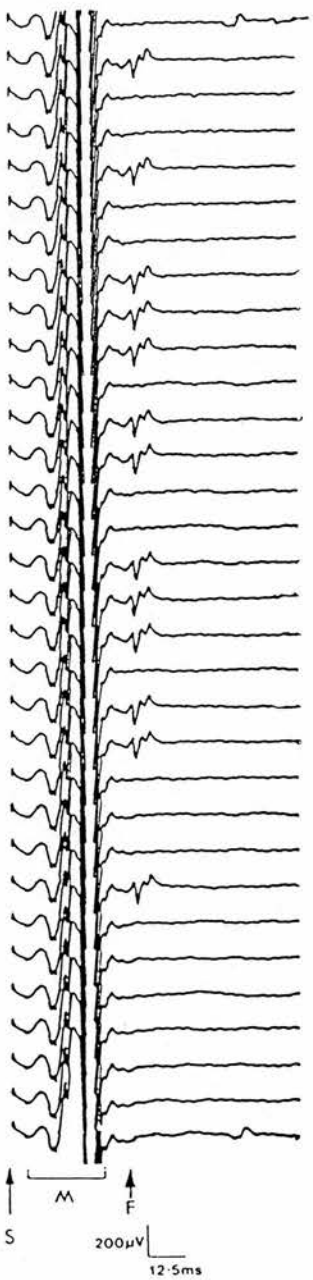


FIGURE 20

REPEATER F-WAVES OF WIDELY DIFFERENT LATENCIES

Two individual Repeater F-waves are present; one appears persistently, the other impersistently.

Recorded from abductor pollicis brevis of a patient with Guillain-Barre syndrome.

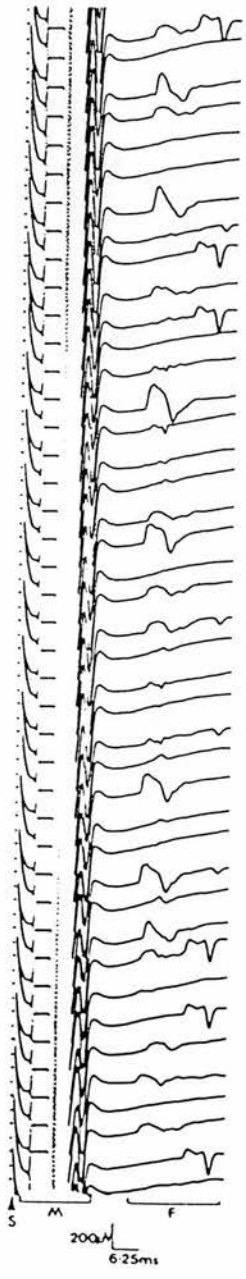


FIGURE 21

"IN SERIES" F-RESPONSES

F-wave sweeps from a patient with cubital tunnel syndrome. The stimulus is applied at the wrist, the recording electrode is over abductor digiti minimi. More than one identifiable F-wave can appear in a single sweep. Two Repeater F-wave types constitute the second of each pair of responses appearing "in series".

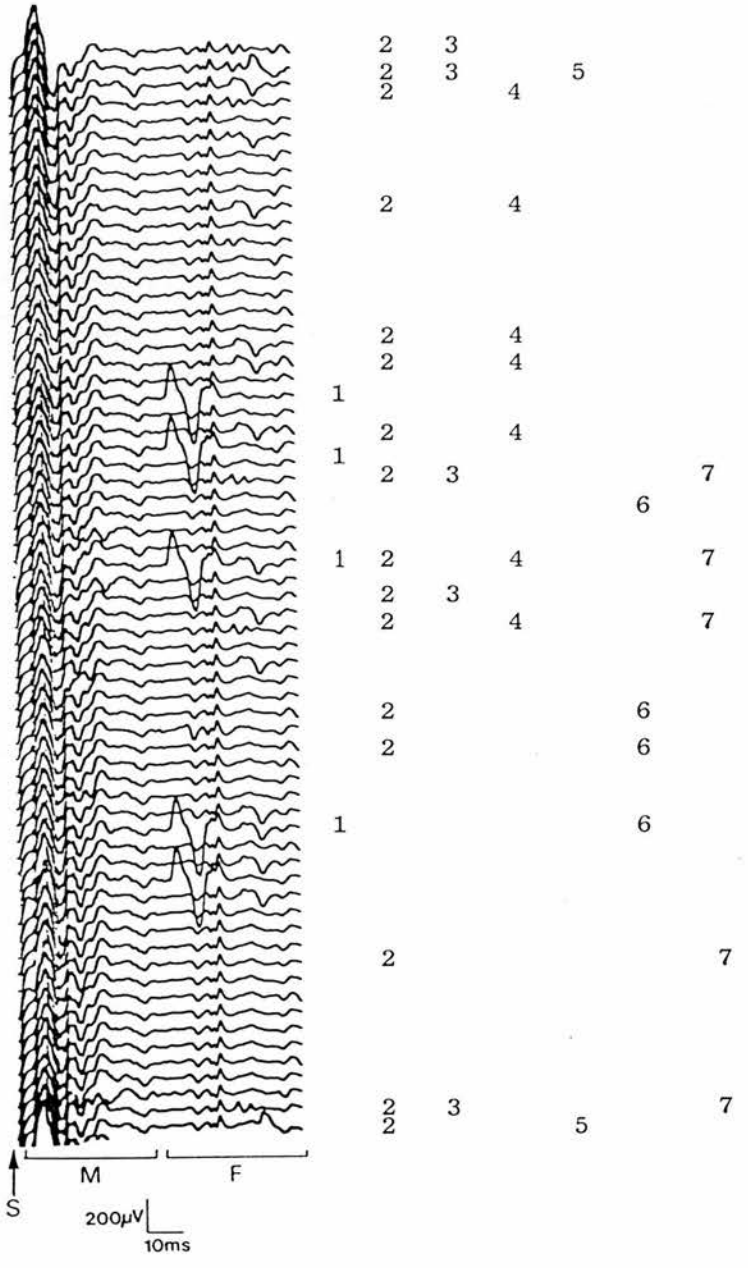


FIGURE 22

REPEATER F-WAVES APPEARING "IN SERIES"

Complex F-wave discharges recorded from abductor pollicis brevis of a patient with Guillain-Barré syndrome. Individual types of Repeater F-waves are indicated by number in some sweeps.

Repeater F-wave no. 2 appears in every sweep while the others are less persistent and appear in varying combinations. F-wave latencies are prolonged and F chronodispersion is pathological. The M wave, also, is dispersed and prolonged. All "late" components in the 'F' bracket had their latencies shortened by moving the stimulus proximally.

4.3.4. Comments and conclusions

The normal pattern of recurrent firing activated by an antidromic volley in a subgroup of segmental motor neurones can be modified by disorders of the peripheral nerve. This is most obvious when a train of stimuli evokes a series of identical F-responses (i.e. %Repeater F-wave value of 100% (Fig. 18[A])). Pathological F-discharges have been recorded from nerves affected by motor neurone disease, Guillain-Barré syndrome, peripheral nerve entrapments, Charcot-Marie-Tooth syndrome, diabetes and alcohol related neuropathy

Both the ulnar and median neuropathy groups displayed two fundamental alterations in their patterns of backfired response to an antidromic volley. Firstly, the subpopulation of anterior horn cells which would normally participate in the F-responses resulting from a series of 100 stimuli appears to be further contracted (waveforms are less variable and, as a group, the damaged nerves produced less persistent F-waves). Secondly, and this was not anticipated, there appears to be facilitation of a restricted fraction of all anterior horn cells for the discharge of recurrent responses. Although F-wave persistence fell in the neuropathy group, that measurement in itself was an insensitive index of dysfunction in a large number of damaged nerves, unless the value was very low, as most had F-persistence values seen in normal range. Ablation of the F-response can occur (subjects seen outside this study) and has always been attended by a greatly reduced M amplitude. Figure 15, (see page 152) shows complete ablation of the F-response 48 hours after the development of paralysis in a patient with Guillain-Barré syndrome. The M amplitude is small suggesting that distal motor conduction block may contribute to the suppression of F-waves. It might be expected that F-wave persistence would be directly proportional to, and that the %Repeater F-wave value would be inversely proportional to the

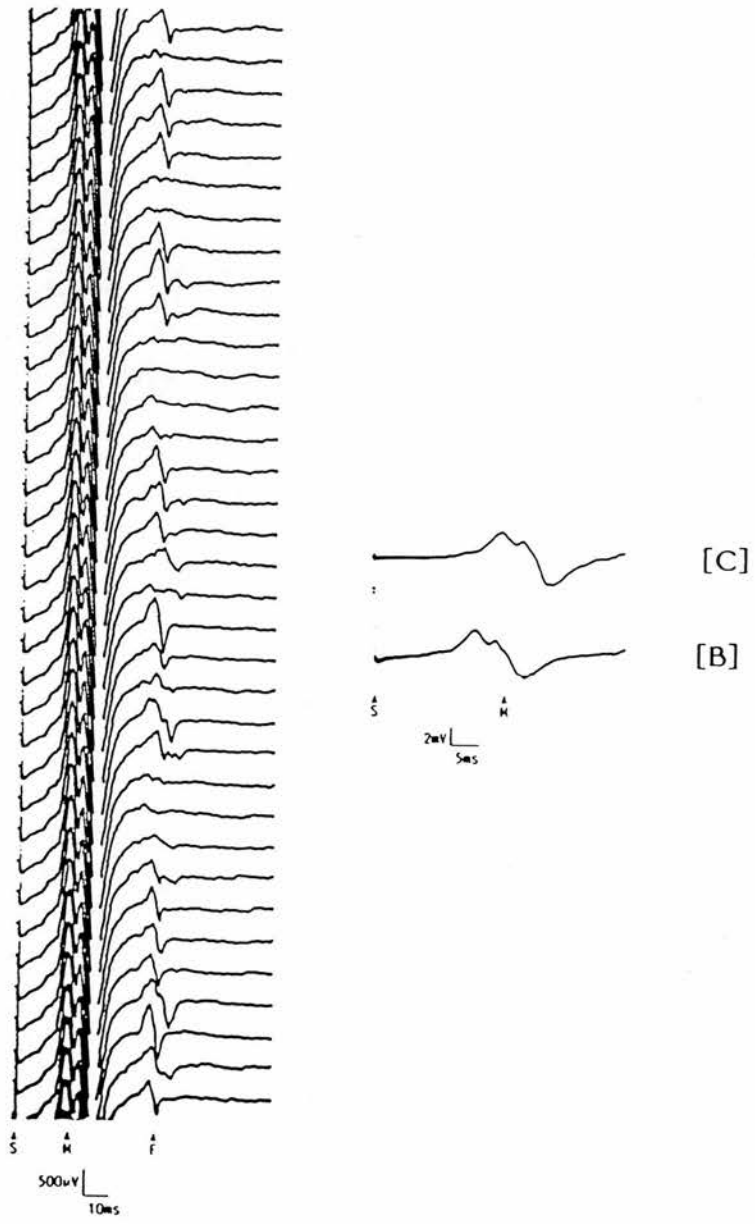
size of the recorded M wave. In individual damaged nerves/muscles this relationship sometimes does not hold. Figure 23 shows a normal %Repeater F-wave value and F-waves occurring at a normal persistence level in a patient with Guillain-Barre syndrome where the M wave is grossly reduced in amplitude. Pathological %Repeater F-wave values can be recorded from muscles with a normal amplitude M wave.

Although the Repeater F-wave count was increased in both groups of damaged nerves compared with the control group, the identification of neural dysfunction in individual nerves can be lost unless the %Repeater F-wave value is calculated, as some damaged nerves produce fewer F-responses than is seen in health.

Not infrequently, damaged nerves were seen to generate Repeater F-waves "in series" and merging Repeater F-waves "in series" may produce complex F-wave forms. Figure 22 shows the type of complex patterns of F-responses which can be recorded. "In series" F-responses were exceptionally uncommon in healthy hands and were never comprised of Repeater F-waves.

Confusion over the interpretation of late responses could arise if either H-reflexes, axon reflexes, or delayed M components were being generated. H-reflexes are abolished by collision in the efferent limb of the reflex arc with antidromic potentials set up by supramaximal shocks and are recorded only exceptionally in the small muscles of the hand (see 3.2). Axon reflexes too are abolished by higher intensity shocks (see 3.5).

It is important that delayed M components are not mistaken for F-responses as demyelinated axons can produce delayed M potentials, in or even beyond, the normal F latency range (Figure 14, see 3.7). Stimulating at a more proximal site shortens the latency of a true F-response and prolongs that of the M and any late M component(s). Figure 24 shows "late" muscle responses evoked by a wrist stimulus in a patient with severe median nerve



[A]

FIGURE 23

A NORMAL F-DISCHARGE PATTERN CONDUCTED THROUGH A PERIPHERAL NERVE IN WHICH THERE IS DISTAL MOTOR CONDUCTION BLOCK

A. Delayed F-waves recorded from the abductor digiti minimi of a patient with acute Guillain-Barré syndrome. F-wave persistence and the Repeater F-wave count fall within normal values.

B. Wrist evoked M wave from the same muscle: Delayed and of low amplitude.

C. Elbow evoked M wave.

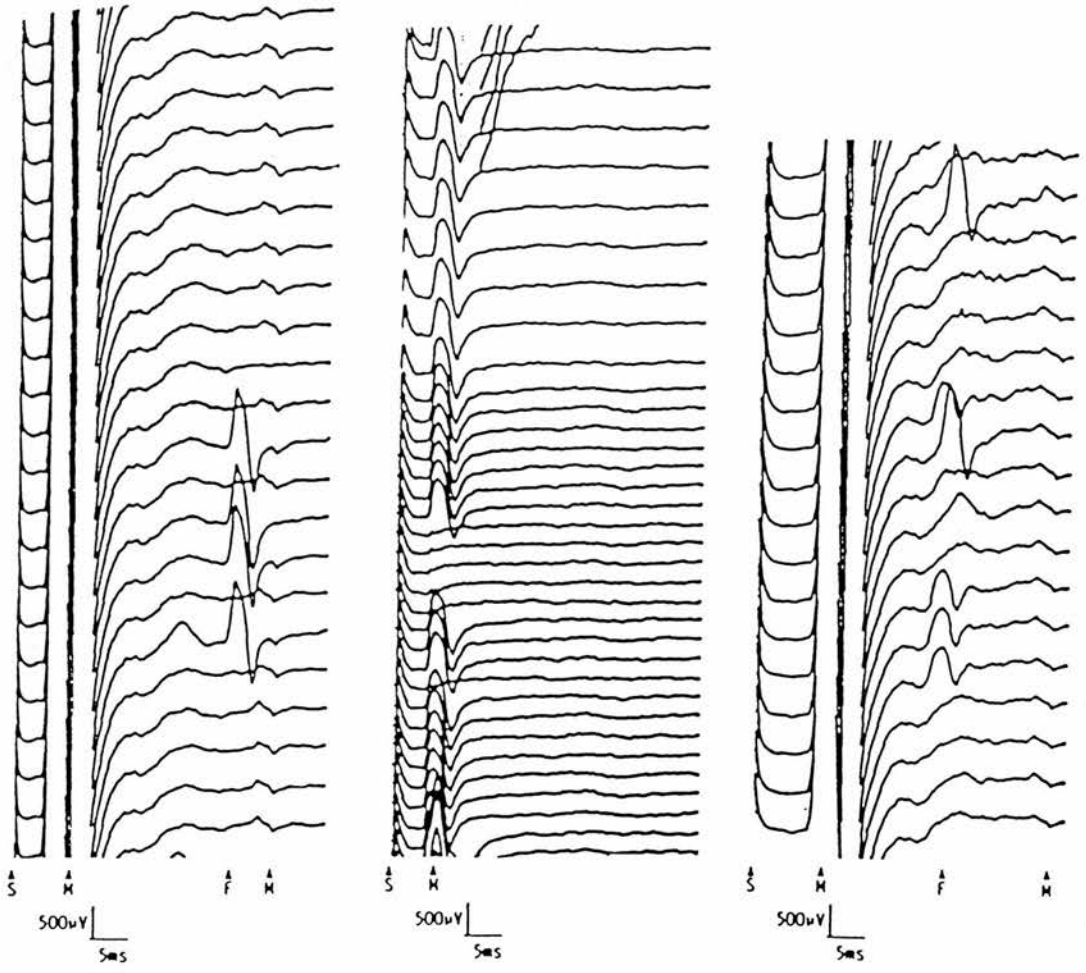


FIGURE 24

A LATE M COMPONENT AND IMPERSISTENT REPEATER F-WAVES RECORDED FROM ABDUCTOR POLLICIS BREVIS; CARPAL TUNNEL SYNDROME

A: A supramaximal stimulus at the wrist evokes a delayed M component (Ca. 38 ms) preceded by a Repeater F-wave (Ca. 33 ms).

B: Submaximal stimuli failed to generate either the slowly conducted M impulse or the impersistent F-responses.

C: Moving the stimulus to the elbow shortens the F-waves' latencies (Ca. 26 ms), (note different individual Repeater F-waves still appear), and lengthens the latency of the late M component (Ca. 44 ms).

dysfunction due to carpal tunnel syndrome. Repositioning the stimulating electrode at the elbow shows that the latest deflection in each sweep arises from orthodromic conduction in slow conducting fibres and that it is not a repeatedly backfired F-response nor an axon reflex.

The voltage used in this study to generate F-responses was 20% supramaximal for the M wave and in only 2 nerves did a single "late" waveform (whose latency was shortened by moving the stimulus proximally) appear in response to 100 consecutive stimuli. Otherwise, when a single Repeater F-wave made up the F-responses from a nerve there were invariably M waves which were not followed by a late response, i.e. almost invariably, highly persistent Repeater F-waves failed to follow each stimulus. The placement of the stimulating cathode on the volar aspect of the wrist and the anode on the dorsal aspect can be used to ensure passage of current through the full thickness of the nerve, but this technique was not used to obtain these data. Once a highly persistent Repeater F-wave was recruited, further voltage increments (>20% supramaximal) made no change in its configuration and did not ablate it. Were intermittent axon reflexes (if such exist) appearing with consecutive stimuli one would expect variable waveform F-waves to be present in addition, whatever the latency of the axon reflex. If the F-waves were of different latencies from the axon reflex(es) the axon reflex waveforms would be stable and variable F-responses would coexist. If F-wave and axon reflex latencies were the same in an individual muscle, the summated potentials would again be variable, as in the case of F-potentials from a healthy nerve. The phenomenon of same-latency, same-waveform "late" responses is not explained by axon reflexes in the damaged nerves, even if they occur intermittently with supramaximal shocks (for which the author can find no evidence). Figure 25 illustrates how a persistent "late" potential can be

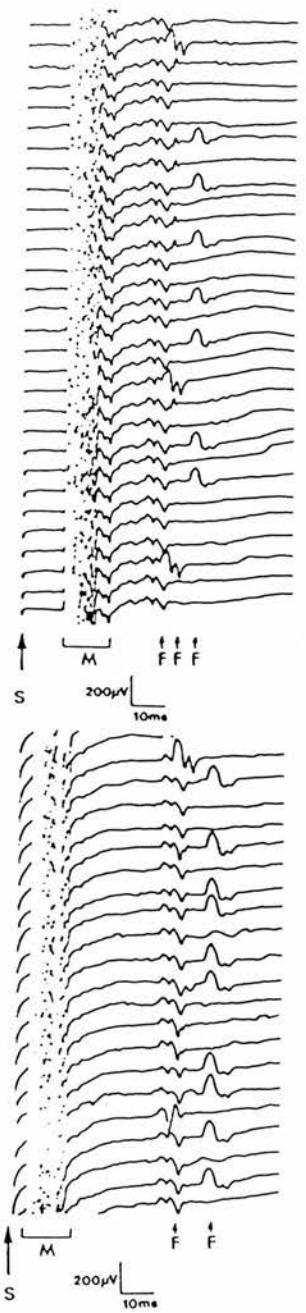
FIGURE 25

M COMPONENT OR PERSISTENT REPEATER F-WAVE?

F-wave sweeps recorded from the thenar eminence of a patient with acute Guillain-Barré syndrome.

A: Wrist stimulus. In [A] the M-wave is followed by, what the author believes to be, several individual Repeater F-waves "in series". The initial "late" response appears in almost every sweep.

B: Elbow stimulus. In [B] it is seen that the highly persistent fastest conducted "late" response recorded in [A] is indeed an F-response not a late M component as its latency is shortened by moving the stimulus proximally. An additional individual Repeater F-wave (recorded once with the wrist stimulus) appears three times. The slowest conducted intermittent, but highly persistent, "late response" also has its latency shortened at the elbow.



shown not to be an M component. Some of these delayed "late" responses are impersistent when activated by a supramaximal shock and can, the author believes, be distinguished from axon reflexes for those reasons (see 3.5). The highly persistent "late" response (the earliest one in each sweep) is also likely to be an F-response in view of the stimulus intensity being used. Some axon reflexes follow, rather than precede the F-wave, if impulses are propagated slowly along the collateral sprout. The latency of any "late" response and shortening of latency with a more proximal stimulus does not distinguish an axon reflex from an F-response. If, however, a late response (typically one following each stimulus) has its latency shortened by moving the stimulus more proximally and then disappears if an even more proximal stimulus is applied, then it can be taken to be an axon reflex.

It should be stressed that the high %Repeater F-wave values recorded in this study came not only from recordings done on denervated muscles with a depleted motor unit stock but also from muscles without any identifiable motor fibre dysfunction (see below).

The subjectivity involved in identifying Repeater F-waves cannot be quantified (although the author is at present developing an automated analysis). However, it is easier to pick out identical waveforms when F-responses are less persistent and when Repeater F-waves appear at a higher, rather than lower, frequency. It is likely, therefore, that there was a bias against the identification of Repeater F-waves in the control population compared with the pathological material.

As an electrodiagnostic parameter the %Repeater F-wave value is non-specific for type and site of peripheral nerve lesions. Clinical findings and associated electrodiagnostic abnormalities would be essential to the correct interpretation of high %Repeater F-wave values.

The interplay of corticospinal and peripheral nerve influences on the spinal motor neurone pool is, of course, extremely complex (see 1.4, 4.1.12, 4.2.1). As well as spinal segmental differences in the pattern of motor neurones' recurrent discharges, there are also differences between the populations of motor neurones in the same spinal segment (see 2.2). For an antidromic impulse to backfire an alpha motor neurone it has to enter the soma and find the soma-membrane in a favourable state of partial depolarisation (Eccles 1955). While central factors are responsible for the intermittent appearance of the F-response, alterations in segmental input caused by peripheral nerve lesions appear to further modify the alpha motor neurones' backfiring capacity: an increased majority of the neurone pool is inhibited while a small minority of neurones is facilitated.

It might be predicted that a disease process such as motor neurone disease, which depletes anterior horn cell numbers, might cut down on the variability of F-responses if F-wave generators became inactive (Peioglou-Harmoussi et al 1987(a)). The unexpected finding is that same-latency, same-shape waveforms occur not impersistently, but at a pathologically high rate from a given motor pool. Two possible explanations for the Repeater F-wave phenomenon, using a theoretical pure motor fibre dysfunction model (a role motor neurone disease does not fulfil) (Norris 1975) will be discussed. Firstly, the usual F-waves seen in health might be composites of two distinct groups of alpha motor neurones with different F-discharge patterns: Group (a) a very small number of motor neurones which issue a recurrent reponse very frequently and which are present in the majority of recorded F-waves, and Group (b), a larger group than (a), whose firing is much less predictable and much less frequent. In health their summation would produce the typical variability of F-waveform and latency. If a disease process removed group (b) units then group (a) would comprise Repeater F-wave responses, i.e. the

finding of persistent identical F-responses would represent an unveiling of activity camouflaged by variable backfiring in another subset of alpha cells. Against this the amplitude of Repeater F-waves is not obviously smaller in the diseased state (and this includes muscles where motor unit territories are not increased by reinnervation) than in health. It is not known if supramaximal stimuli can backfire a subset of motor neurones at high persistence. (the single motor unit F-wave persistence studies of Schiller and Stålberg (1978) used shocks submaximal for the M wave). This model would additionally be unacceptable if there were no motor fibre dysfunction associated with a pathological %Repeater F-wave value (see below).

Alternatively, a subgroup of anterior horn cells might be selected out from the usual pool of F-wave generators and those cells fire at a pathological frequency. Such facilitated activity in one group of motor neurones might be associated with inhibition in others. How this might be effected is obscure but a number of possible mechanisms will be discussed.

It is apparent that while the size of the motor neurone pool remains constant for an individual nerve/muscle under test the %Repeater F-wave value can be modified by altering the composition of the centripetal volley. Figure 26 shows an individual late response, (X), (2 left hand sets of sweeps, 200 μV gain and 100 μV gain) recorded from abductor digiti minimi with the stimulus at the wrist in a patient with an ulnar nerve lesion at the elbow. (X) appears persistently with this stimulus, (%Repeater F-wave value nears 100%), but when the stimulus moves above the elbow (2 right hand sets of sweeps) the late response pattern changes; additional Repeater F-waves appear and (X) is less persistent. The number of motor units in abductor digiti minimi if fixed while some variable(s) affecting their backfired discharge pattern is/are changed. The composition of the antidromic volley has been changed in many ways by moving the stimulus proximally, e.g.

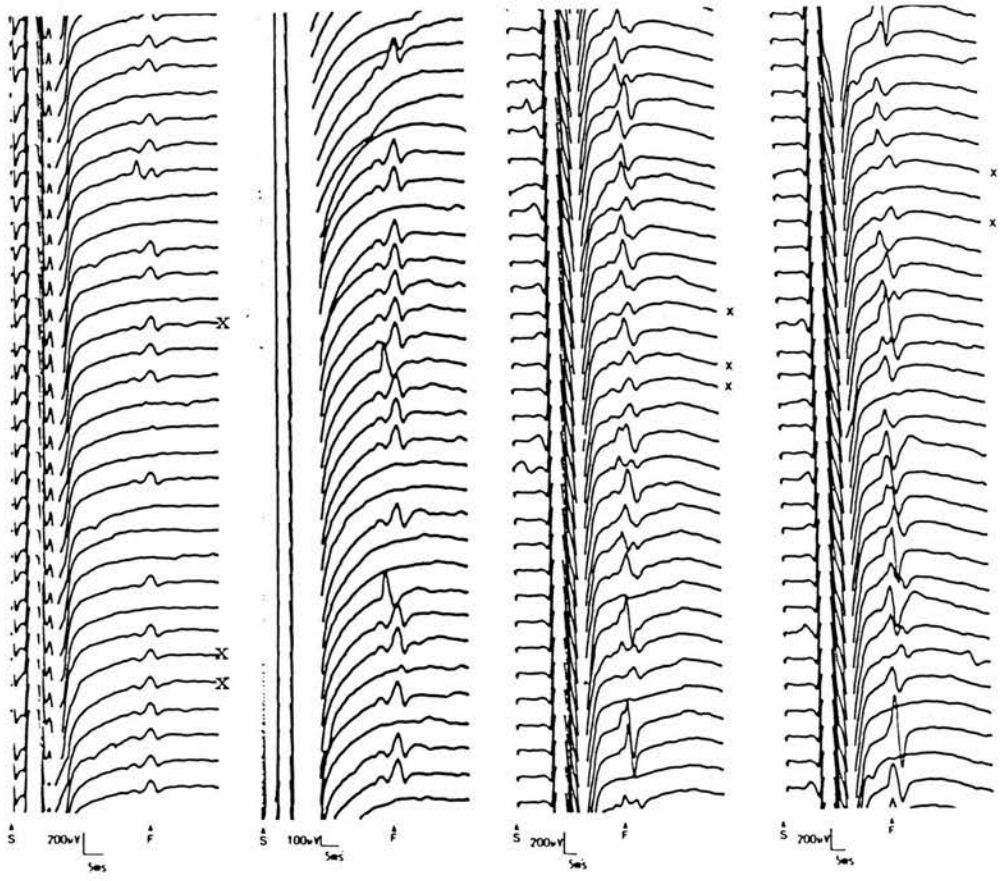


FIGURE 26

ULNAR NERVE LESION AT THE ELBOW

F-responses recorded from abductor digiti minimi.

A,B: With the stimulus applied to the ulnar nerve at the wrist a persistent Repeater F-wave (X) follows the majority of stimuli at 27 ms [B higher gain].

C,D: When the stimulus is moved proximal to the elbow the Repeater F-wave (X) becomes less persistent and its latency shortens to 23 ms.

The %Repeater F-wave value obtained with the stimuli delivered above the lesion is no longer outside the control reference range (for wrist stimulation).

motor fibres and spindle afferents from flexor carpi ulnaris and additional cutaneous afferents are now activated and will influence Renshaw inhibition and sensory inputs onto the motor neurones subserving abductor digiti minimi. The temporal profile of the impulses in the abductor digiti minimi axons, themselves, will be different on reaching the spinal cord from the two sites. (The findings in Figure 26 are taken as a further indication that the response (X) from the wrist is not an intermittent axon reflex (if there is such an entity).

In many of the damaged nerves included in this study both motor and sensory fibre dysfunction were present and sensory, as well as motor, fibre dysfunction may contribute to the finding of high %Repeater F-wave values through a variety of obscure mechanisms. Animal experiments have shown that Ia afferents impinge on motor neurones both directly and through spinal interneurones, some of which may be inhibitory (Fetz et al 1979, Jankowska et al 1981). The mono-synaptic and oligo-synaptic effects of sensory afferences on the test motor neurones in these experiments is extremely complex but it is likely, at least, that Ia impulses will influence the liability of motor cells to discharge F-waves (Delwaide 1973). As well as the fastest conducting afferents, cutaneous afferents have been shown to influence the excitability of soleus motor neurones as tested by the H-reflex (Gassel and Ott 1970). The role these afferences might have in controlling F-wave production is harder to predict. One might speculate that they could be relevant to smaller slower conducting motor neurones or be relevant to F-wave production if motor conduction was slowed.

It is possible that through a change in the profile of the sensory volley, which accompanies the test antidromic motor volley, the population of motor cells capable of issuing an F-response at the time of arrival of the motor impulses will be altered from normal, i.e. the membrane potentials

could be modified from normal to permit or prevent a backfired response.

The derepression of motor neurones permitting them to issue F-responses could also be an important mechansim relating to the experimental findings. In health, fastest alpha axons conduct the minimal latency F-responses (Shahani et al 1987). These large diameter fibres are particularly susceptible to pressure damage (cf. muscle spindle afferents) and it is conceivable that dysfunction in a fraction of these fibres could have a significant impact on the Renshaw inhibition of the motor neurone pool in compression neuropathy. (But it was seen that F-response patterns were unaltered in a significant number of the subjects with cubital tunnel syndrome). The first impulses of the antidromic volley to initiate Renshaw cell mediated motor neurone inhibition are those transmitted by the fastest conducting axons. In health, the tight latency spread of F-responses may, in part, be due to the inhibition of slower conducting motor neurones by the volley in the fastest conducting ones. If a partial lesion of fastest, and largest diameter alpha neurones led to a loss of the usual Renshaw mediated inhibition on smaller cells then those with suitable depolarising/repolarising schedules could be those which act as Repeater F-wave generators. Conduction block affecting fastest alpha axons would also obliterate the second wave of Renshaw inhibition which would otherwise have occurred through those cells' Renshaw loop if an F-wave had been transmitted, i.e. the inhibitory effect induced by the F-wave discharge through its own Renshaw cell will be lost.

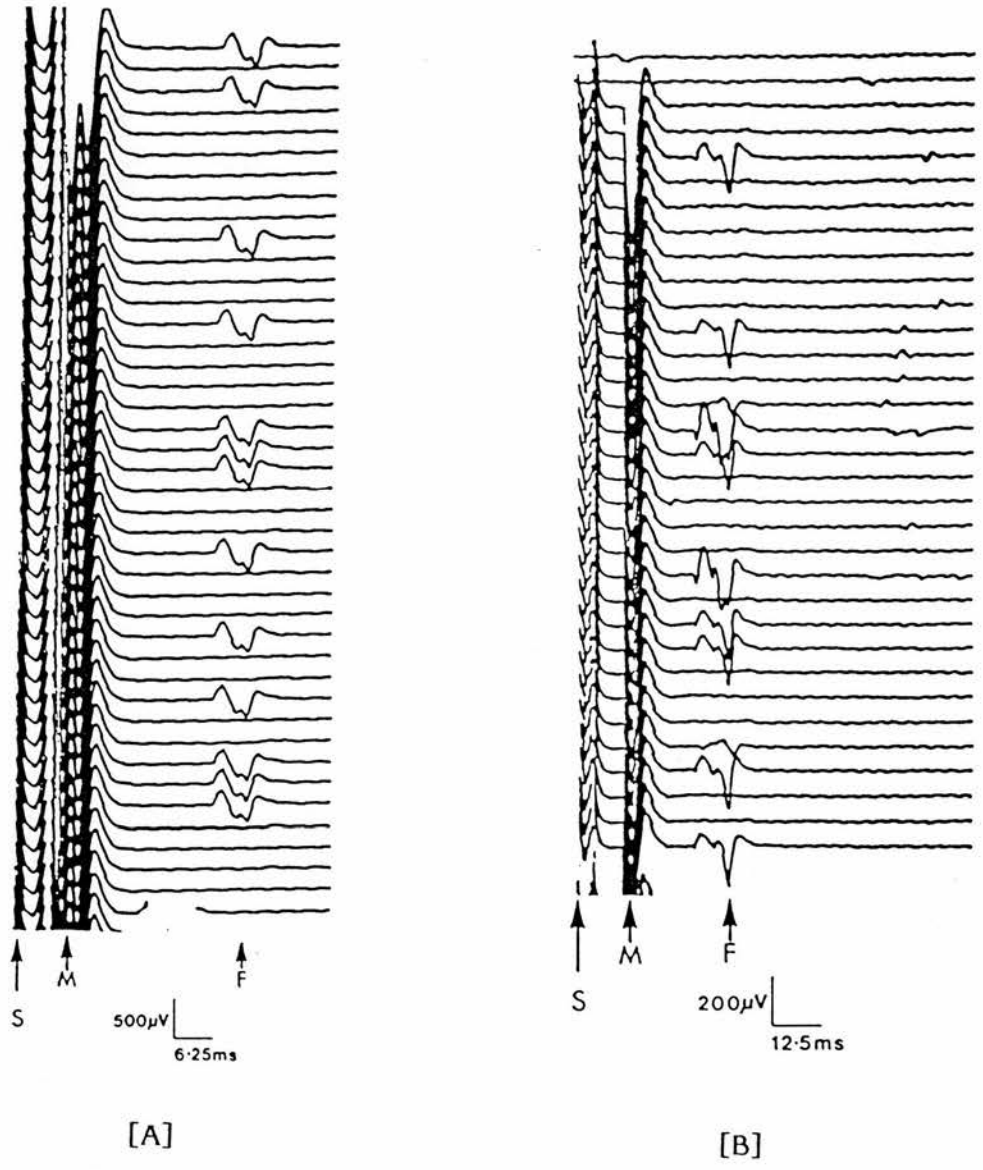
Central predeterminants exist, therefore, in the selection of motor cells which are capable of acting as Repeater F-wave generators (Fisher 1979). Pathological patterns of F-wave production can be seen in acute neuropathies e.g. <48 hours onset of paralysis in Guillain-Barré syndrome, where time for structural reorganisation is absent. This suggests an

underlying functional basis for the findings in those instances.

The absence of an obvious direct relationship between the M wave's amplitude (relating to the number of intact motor units in a test nerve/muscle) and the F-wave persistence and %Repeater F-wave values in some muscles is noteworthy. Whether it indicates that a peripheral sensory fibre lesion may be important in determining F-wave production is unclear.

The findings of these experiments suggest that peripheral neuropathies and neuronopathies can be identified by quantifying F-wave discharge patterns using the %Repeater F-wave measurement. The %Repeater F-wave parameter offers an alternative to pure latency testing for surface based electrodiagnosis. It would appear to have a complementary role to conventional techniques as it quantifies a distinct aspect of neural dysfunction. The author has recorded F-responses with pathological %Repeater F-wave values when other conventional surface-based nerve conduction study techniques have revealed no abnormality. Two will be mentioned for illustrative purposes. Figure 27 shows F-wave sweeps from intrinsic hand muscles of 2 patients whose conventional electrodiagnostic examination (sensory and motor nerve conduction studies, blink reflexes and EMG) revealed no abnormality. Case A (KO, Tayside Health Board no. 150749), a woman in her 30's presented with ocular and neuro-sarcoidosis. She had subjective sensory disturbances, but no signs in her hands. Case B, presented with a fasciculating tongue, dysarthria and dysphagia. There were no clinical or EMG signs of a neuronopathy affecting her hands when these F-responses were recorded, but she later died with extensive motor neurone disease.

The sensitivity of the %Repeater F-wave measurement, compared with conventional nerve conduction study measurements in the detection of peripheral nerve lesions, will be considered separately in 6.5.



[A] [B]

FIGURE 27

A: Neurosarcoidosis

100% Repeater F-wave value recorded from abductor pollicis brevis - single, highly persistent, individual Repeater F-wave.

B: Progressive bulbar palsy

100% Repeater F-wave value recorded from abductor digiti minimi - 3 individual Repeater F-waves.

4.4. Pathological F-wave Discharge Patterns in Miller-Fisher Syndrome

4.4.1. Introduction

Uncertainty and controversy exist over the pathophysiological mechanisms underlying the clinical syndrome of ataxia, areflexia and ophthalmoplegia (Ropper 1983, Meienberg 1984). Fisher (1956), in the original description of the syndrome, reluctantly interpreted all the clinical signs as an unusual disturbance of peripheral neurones, although, conventionally, the midline type of ataxia and panophthalmoplegia are more suggestive of a central disturbance of nervous system function. The possibility that the midline ataxia and opthalmoplegia could arise from lesions outside the central nervous system is intriguing and the concept of a disordered peripheral nervous system generating "counterfeit" central nervous system physical signs is an important one to remember in the practice of clinical neurology and electrodiagnosis (Glaser 1966).

Neuropathological case reports are few, and in one, the authors suggested that the syndrome should be regarded as an inflammatory polyneuropathy despite failing to include the distal portions of the third, fourth and sixth cranial nerves in the examination (Phillips et al 1984). In that case report, the microscopic examination of the spinal nerve roots, peripheral nerves and cranial nerves revealed patchy, but extensive, recent segmental demyelination. The proximal portions of the third, fourth and sixth cranial nerves, the brain stem and the cerebellum showed no abnormalities.

There are only a few reports of abnormalities of peripheral nerve conduction in the Miller-Fisher Syndrome (Elizan et al 1971, Guiloff 1977, Jamal and Macleod 1984).

The absence of central nervous system lesions is suggested by necropsy reports from Grunnet and Lubow (1972) and Phillips and colleagues (1984).

The author has encountered two cases of Fisher syndrome (one of which is described below) in which CT and MRI of the brain stem and cerebellum (kindly performed by Dr Graham R. Cherryman at Aberdeen Royal Infirmary) showed no abnormality using T1 weighted images. While of interest, the MRI examination lacked T2 weighted images and can be, at best, inconclusive. However since then, a personal communication from Dr Allan Ropper, Massachusetts General Hospital, Boston, has indicated that both T1 and T2 weighted magnetic resonance images of brain stem in several cases of the syndrome have also failed to identify an intrinsic brain stem lesion.

One case will be described here in which conventional conduction studies failed to show an abnormality of the peripheral nervous system but in which abnormalities of the F-wave discharge patterns were detected in the upper limbs.

4.4.2. Case report

A previously fit 48 year old female Dutch tourist, P.O.V. (Tayside Health Board No. 210237) developed acute ataxia, diplopia and dysarthria during a holiday in Dundee and presented to the author via the casualty department on 28/7/85.

On examination there was an, almost complete, external opthalmoplegia. Doll's eye movements were lost while pupillary reactions to light were retained. She was unable to sit, stand or walk without support due to a gross midline ataxia. Contrastingly, the performance of finger-nose and heel-shin tests was excellent. The right triceps reflex was abolished. There

was a flaccid bulbar dysarthria. There was no impairment of power in the muscles innervated by the facial and trigeminal nerves and the limbs were strong.

CT and MRI (performed by Dr G. Cherryman, Aberdeen Infirmary) of the brain stem showed no intrinsic lesion. Cerebrospinal fluid protein concentration was slightly increased at 518 mg/l only just above the upper limit of normality for the hospital's laboratory. There was no CSF pleocytosis. Conventional nerve conduction studies, which included motor evaluation of the median, ulnar and peroneal nerves and sensory evaluation of sural, median and ulnar nerves showed no abnormality (this included F-wave latencies).

%Repeater F-wave values obtained from 2 of 4 intrinsic hand muscles tested were outwith the control ranges. Figure 28 shows a pathological F-wave pattern recorded from one abductor digiti minimi muscle.

As the clinical recovery took place, the abnormal F-response patterns reverted to normal.

4.4.3. Comment

It has been suggested that afferent nerve defects might provide a reasonable explanation for the cerebellar ataxia of Fisher syndrome (Ropper and Shahani 1983). In the ataxic form of acute post-infective polyneuropathy, a patient reported by Richter (1962) had a normal brain stem and cerebellum at autopsy, but had abnormalities of fibres passing through Clarke's column. The abnormalities of the F-discharge patterns in P.O.V. were not associated with conventional nerve conduction study abnormalities. They could represent either a primary dysfunction within the peripheral nerves (be it root, plexus and/or peripheral nerve) or a primary dysfunction

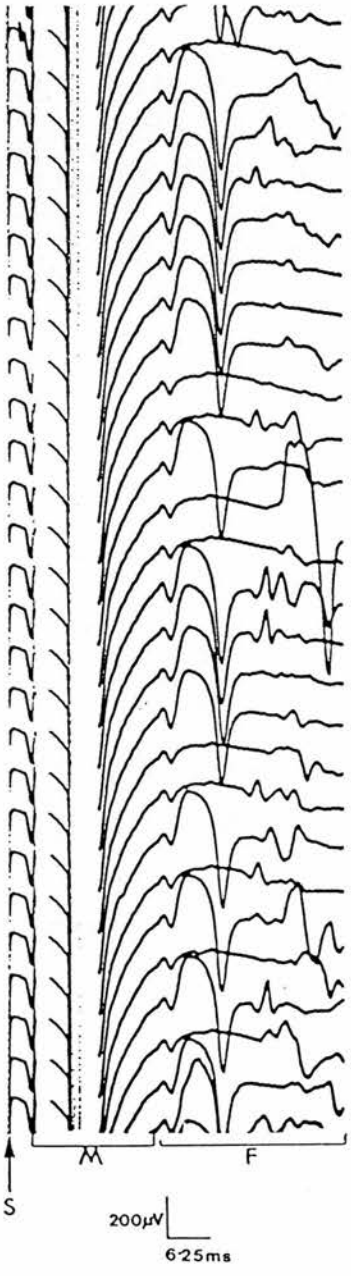


FIGURE 28

MILLER FISHER SYNDROME

Pathological F-responses recorded from the abductor digiti minimi muscle of a patient with Fisher's syndrome.

in the central nervous system, i.e., could represent altered physiological behaviour within the spinal cord. The same reversible alteration in F-wave generating activity has been seen in another case of Fisher syndrome when conventional nerve conduction studies and CT/MRI appearances in the brain stem and cerebellum were normal. It is of interest to observe these changes in view of the possibility that Fisher's syndrome might represent a disorder of function (without concomitant structural changes) in the central or peripheral nervous system. The F-wave generating abnormalities are, however, non-specific and do not allow any new conclusions to be drawn about the underlying mechanisms in the syndrome.

4.5. Pathological %Repeater F-wave Values Resulting from Intraspinal Lesions

The author has studied a small number of cases of cervico-dorsal syringomyelia with hand wasting. Most of the patients had attended the Department of Neurosurgery at Dundee Royal Infirmary.

Thenar and hypothenar %Repeater F-wave values were found, in some, to be higher than the maximum observed in the control range, while no features diagnostic of a secondary mixed nerve entrapment syndrome were identified.

A large enough series has not been assimilated for a meaningful analysis and therefore the findings in a single case will be documented to show that an ipsisegmental intraspinal lesion can modify F-wave discharge patterns of the motor nerves supplying the intrinsic hand muscles just as a lesion in the mixed peripheral nerve can. This patient was referred to the EMG Laboratory in The Massachusetts General Hospital where the author evaluated him (the case was included in a presentation to the American Academy of Physical Medicine and Rehabilitation, in Orlando, Florida in 1987, and my coauthor was Dr B.T Shahani whose interest in the case concerned high frequency repetitive discharge recorded from myotomes of the damaged cord segments (Macleod and Shahani 1987)).

SA, a 65 year old man, presented with gradually progressive, widespread wasting in his left upper limb. It affected his hand, forearm, shoulder and periscapular muscle clinically. A diagnosis of syringomyelia was thought to be likely from associated sensory features and was ultimately confirmed by myelography and surgery.

Nerve conduction studies revealed no evidence of a postganglionic sensory fibre lesion and motor nerve conduction velocities in the forearm segments of the ulnar and median nerves were normal (Table 20).

F-wave latencies from abductor pollicis brevis were delayed (see contralateral values). Electromyography revealed that denervation and reinnervation extended rostrally from the thin hand to the left sterno-deidomastoid muscle, but blink reflex latencies showed no delays of transmission. Figure 29 shows the pattern of F-responses recorded from the wasted left abductor pollicis brevis muscle. The %Repeater F-wave value was pathological.

Comment. There are a number of pathological anatomical features present in the spinal cord of this patient which might be relevant to the finding of a pathological F-wave discharge pattern. The size of the test motor neurone pool is reduced (loss of anterior horn cells) and there may be disruption of a variety of types of intraspinal connections. Those abnormalities could result in an alteration from the normal of the membrane potentials of the remaining motor neurones and hence in thier F-wave generating behaviour. No evidence was seen of a peripheral entrapment syndrome affecting the left median nerve and it is likely that the primary intraspinal pathology has resulted in this modified F-discharge pattern.

TABLE 20

NERVE CONDUCTION STUDY AND ELECTROMYOGRAPHIC STUDY OF S.A.: A CASE OF CERVICO-DORAL SYRINGOMYELIA

KEY: E.M.G. motor unit recruitment patterns -

High mixed	:	Full recruitment
Mixed	:	Slightly reduced recruitment
Low mixed	:	Clearly reduced recruitment

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Electromyography :
Laboratory :
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SA
UNIT NUMBER : 183-30-30
SEX : MALE
BIRTH DATE : 07/23/21

RE UNIT : POP (PRIVATE OUT-PATIENT)
ST DATE : FRIDAY 3 APRIL 1987 TEST NUMBER: 1
DERED BY : DR. POLETTI

erring Diagnosis:

ght : 75 Kilograms
ght : 180 Centimeters
face Area: 1.94 Square Meters

Limb Temperatures in Degrees Celsius

	RIGHT	LEFT
ARM		
LEG		

Motor Nerve Conduction Studies

Distance / Latency / Amplitude / Duration / Conduction Velocity					
	cm	msec	uV	msec	M/sec
-> LEFT MEDIAN MOTOR NERVE -- ABDUCTOR POLLICIS BREVIS					
WRIST	7.0	4.00	3500	7.400	
Comment->	LOW AMPLITUDE				
Remarks->	ABNORMAL				
ELBOW	23	8.00	3500	8.000	58
Comment->	LOW AMPLITUDE				
Remarks->	ABNORMAL				
-> LEFT ULNAR MOTOR NERVE -- ABDUCTOR DIGITI MINIMI					
WRIST	7.5	3.00	9000	7.200	
Remarks->	NORMAL				
BELOW ULNAR GROOVE	24	7.50	9000	7.300	53
Remarks->	NORMAL				

Continued on Page # 2

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Laboratory :
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SA
UNIT NUMBER : 183-30-30
SEX : MALE
BIRTH DATE : 07/23/21

Sensory Nerve Conduction Studies

Distance ---------->	cm		Evoked Response		
Latency ---------->	msec				
Amplitude ---------->		uV			
Duration ---------->			msec		
Conduction Velocity ---------->					M/sec
--> LEFT RADIAL SENSORY NERVE -- DIGIT I					
WRIST	13	2.40	7.000	2.400	54
Remarks->	NORMAL				
--> LEFT ULNAR SENSORY NERVE -- DIGIT V					
WRIST	14	2.60	8.000	3.800	54
Remarks->	NORMAL				

Mixed Nerve Conduction Studies

Distance ---------->	cm		Evoked Response		
Latency ---------->	msec				
Amplitude ---------->		uV			
Duration ---------->			msec		
Conduction Velocity ---------->					M/sec
--> LEFT MEDIAN MIXED NERVE -- PALM					
WRIST	8.0	1.30	125.0	2.200	62
Remarks->	NORMAL				

Electromyography

	Spontaneous Activity		Voluntary Activity		
Fibrillations ---------->					
Fasciculations ---------->					
Amplitude ---------->		uV			
Duration ---------->			msec		
Polyphasics ---------->					%
--> LEFT ARM <--					
BICEPS	2+	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW MIXED				
remarks->	ABNORMAL				
BRACHIORADIALIS	0	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW MIXED				
remarks->	ABNORMAL				
ABDUCTOR DIGITI MINIMI	2+	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW MIXED				
remarks->	ABNORMAL				

Continued on Page # 3

ssachusetts General Hospital :
Electromyography :
Laboratory :
nted on 04/03/87 at 5:16 PM :

SA
UNIT NUMBER : 183-30-30
SEX : MALE
BIRTH DATE : 07/23/21

Electromyography

	Spontaneous Activity		Voluntary Activity		
ibrillations ---------->					
asciculations ---------->					
mplitude ---------->		uV			
uration ---------->			msec		
olyphasics ---------->					%
MID DELTOID	0	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW	MIXED			
remarks->	ABNORMAL				
--> LEFT HEAD AND NECK <--					
STERNOCLEIDOMASTOID	0	1+	H	PROLONGED	HIGH %
recruitment pattern->	MIXED				
remarks->	ABNORMAL				
SUPERIOR ORBICULARIS ORIS	0	0	NORMAL	NORMAL	
recruitment pattern->	HIGH	MIXED			
remarks->	NORMAL				
--> LEFT TRUNK <--					
SERRATUS ANTERIOR	2+	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW	MIXED			
remarks->	ABNORMAL				
SUPRASPINATUS	0	1+	H	PROLONGED	HIGH %
recruitment pattern->	LOW	MIXED			
remarks->	ABNORMAL				

Late Response Studies

istance ---------->	cm					
ax Latency ---------->		msec				
in Latency ---------->			msec			
mplitude ---------->				uV		
uration ---------->					msec	
ercentage Persistence ---------->						%
--> RIGHT MEDIAN NERVE -- ABDUCTOR POLLICIS BREVIS -- F RESPONSE						
RIST	72	25.0	23.0			
Remarks->	NORMAL					

Continued on Page # 4

sachusetts General Hospital	SA
Electromyography	UNIT NUMBER : 183-30-30
Laboratory	SEX : MALE
nted on 04/03/87 at 5:17 PM	BIRTH DATE : 07/23/21

Late Response Studies

	Distance	Max Latency	Min Latency	Amplitude	Duration	Percentage Persistence
	cm	msec	msec	uV	msec	%
-> LEFT MEDIAN NERVE -- ABDUCTOR POLLICIS BREVIS -- F RESPONSE						
RIST	72	32.0	30.0			
Comment->	PROLONGED					
Remarks->	ABNORMAL					
-> LEFT ULNAR NERVE -- ABDUCTOR DIGITI MINIMI -- F RESPONSE						
RIST	72	32.0	30.0			
Remarks->	ABNORMAL					

Blink Reflex Studies

	Latency msec	Amplitude uV	Duration msec	Comment
-> RIGHT SUPRAORBITAL NERVE -- IPSILATERAL ORBICULARIS OCULI				
IRST COMPONENT	10.0	500.0	10.00	NORMAL
ECOND COMPONENT	35.0	1000	35.00	NORMAL
-> RIGHT SUPRAORBITAL NERVE -- CONTRALATERAL ORBICULARIS OCULI				
ECOND COMPONENT	35.0	775.0	35.00	NORMAL
-> LEFT SUPRAORBITAL NERVE -- IPSILATERAL ORBICULARIS OCULI				
IRST COMPONENT	10.0	500.0	10.00	NORMAL
ECOND COMPONENT	36.0	400.0	25.00	NORMAL
-> LEFT SUPRAORBITAL NERVE -- CONTRALATERAL ORBICULARIS OCULI				
ECOND COMPONENT	37.0	150.0	10.00	NORMAL

--- IMPRESSION ---

Continued on Page # 5

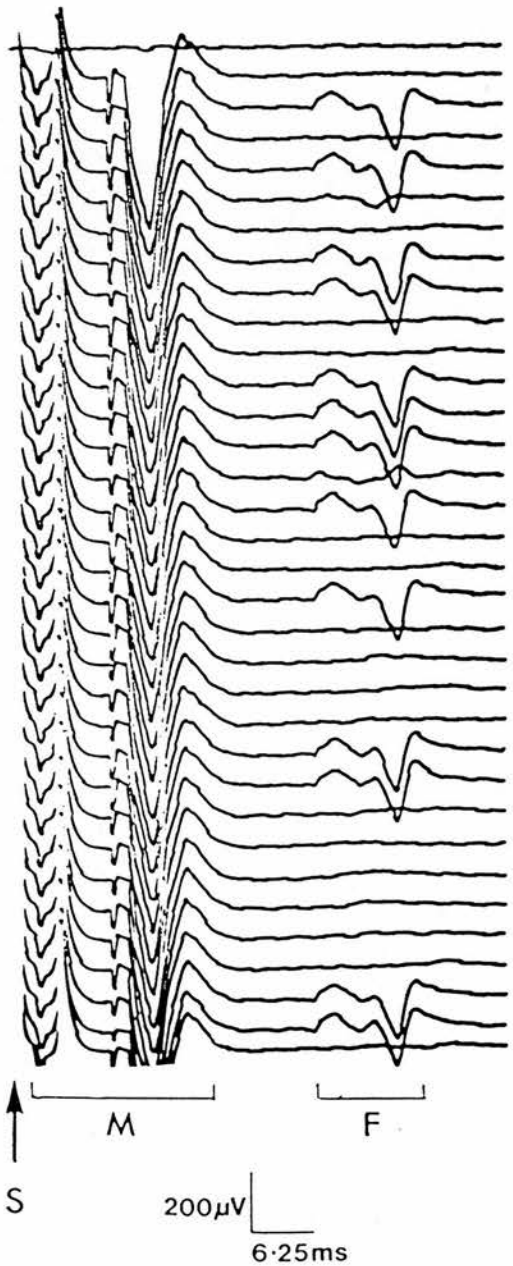


FIGURE 29

CERVICAL SYRINGOMYELIA

100% Repeater F-wave value (1 individual Repeater F-wave type) from the patient's left abductor pollicis brevis.

CHAPTER 5

CHAPTER 5

WAYS OF CALCULATING AND APPLYING THE %REPEATER F-WAVE VALUE IN ELECTRODIAGNOSIS

5.1. Introduction

It is seen from the results of experiments described in Chapter 4 that disorders of the peripheral nervous system can modify the F-wave generating activity of alpha motor neurones. If the %Repeater F-wave value were to be applied as an electrodiagnostic measurement in the EMG laboratory two important questions immediately arise. The first concerns the sensitivity of the technique. Can the %Repeater F-wave measurement be used as a sensitive indicator of peripheral nerve dysfunction? If so, and of particular importance, can pathological F-response patterns occur in the absence of conventional nerve conduction study abnormalities? Secondly, if the method were to be used by clinical neurophysiologists would it be necessary to use trains of as many as 100 stimuli to quantify F-response patterns?

This chapter contains two sets of experiments which address these points separately.

5.2. Is it Necessary to Use as Many as 100 Stimuli to Quantify F-responses? - An Experiment

5.2.1. Introduction

The stimulus intensity used to quantify the F-response patterns in the preceding experiments were surprisingly well tolerated by the volunteers and patients alike. Some patients, however, did find the period of 100 seconds of 1 Hz supramaximal stimulation very uncomfortable. If more than one nerve is stimulated in this way with these rather large numbers of stimuli the patient (usually the younger ones, those who are feeling unwell with either an acute or chronic illness, and often patients with carpal tunnel syndrome) may be intolerant of the procedure, particularly if it forms a small element in a protracted assessment using electromyography as well as nerve conduction studies. Another drawback to using these long trains of stimuli to quantify F-wave generating behaviour, is the expense of photographic paper necessary for such an analysis.

With patient comfort and economy in mind, an analysis was done to see if comparable results were obtained when F-wave generating activity was quantified using briefer trains of stimuli.

To see if the use of smaller numbers of test stimuli, rather than the 100 stimulus paradigm, was associated with a systematic bias in the calculation of the %Repeater F-wave value, results obtained from the same groups of nerves using trains of 30, 60 and 100 stimuli were compared. The collected data was also analysed to determine estimates of imprecision of the methods using smaller numbers of F-wave sweeps to calculate the %Repeater F-wave value.

5.2.2. Methods and subjects

Subjects - The %Repeater F-wave values derived from two test groups were studied: the first group contained nerves/muscles from a population of healthy volunteers and the second group contained damaged nerves from patient volunteers. One hundred and twenty-four median nerves from 87 healthy volunteers (51 female, 36 male, aged 21-72 years) were tested. One hundred dysfunctioning median nerves from 60 patients with carpal tunnel syndrome and 13 patients with thenar wasting, due to motor neurone disease, were tested. The patients with carpal tunnel syndrome all had symptomatic hands (and sometimes arms) and all had abnormalities of the sensory antidromic wrist-palm latency (i.e. a value beyond the upper limit seen in the control population of Dundee Royal Infirmary's EMG laboratory) (see 6.5). An electrodiagnostic abnormality was sought simply to confirm the presence of median nerve fibre dysfunction before inclusion into the study. Some of these patients with carpal tunnel syndrome had motor fibre abnormalities (e.g. prolonged distal motor latency or F-wave latency abnormalities) and some did not. Some patients had thenar wasting, and some did not. Some had electromyographic evidence of subclinical denervation and some did not. The ages of these patients (of which 41 were female and 32 were male) ranged from 31-69 years. They were selected from larger groups of patients with carpal tunnel syndrome and motor neurone disease to include the full range of pathological %Repeater F-wave values, from borderline values to the 100% value (using 100 stimuli). The %Repeater F-wave values obtained with 100 stimuli from the majority of these patients are used in other analyses contained in the thesis.

Methods - F-responses were recorded from the motor point of each abductor pollicis brevis muscle under test. The method for eliciting and recording F-responses is detailed in 2.2, and will not be repeated in full. The type of equipment (electromyographs, electrode types, recording techniques, temperature control and electrode placements) were the same as described in 2.2.

In brief, for each test nerve/muscle 100 supramaximal stimuli were applied at 1 Hz and the %Repeater F-wave value (for the method of calculation of this value see 2.3) was calculated using (a) the first 30 of the 100 F-wave sweeps photographed from the oscilloscope, (b) the first 60 of the 100 photographed F-wave sweeps, and (c) all 100 photographed F-wave sweeps.

Statistical methods

The data from the group of apparently healthy nerves and the data from the group of damaged nerves were analysed separately using the same statistical methods. In both groups the methods used were as follows.

To determine if the calculation of the %Repeater F-wave value from the first 30 rather than the full train of 100 F-responses was associated with a systematic bias, measurements were made on each individual using the first 30 and the full set of 100 stimuli. The observed value obtained from the first 30 stimuli was subtracted from the observed value obtained from all 100 stimuli in each test nerve and a paired t-test was applied to the resulting differences found in each nerve in the test group. The same statistical analysis was done on the %Repeater F-wave values obtained using the first 60 F-response sweeps and the full set of 100 F-response sweeps. This was followed up by calculating the 95% confidence interval for the magnitude of the bias resulting from a method which incorporated 30 or 60

stimuli rather than 100 stimuli.

As well as seeing if a systematic bias resulted from calculating the %Repeater F-wave value from the first 30, rather than the 100 F-wave sweeps or from the first 60 of the full set of 100 F-wave sweeps, the imprecision of each of these methods was also considered. To estimate the imprecision of the method using 30 stimuli to calculate the measurement, the standard deviation of the differences between the measurements obtained using 30 stimuli and 100 stimuli in each of the individual test hands in the group was calculated (the same sort of analysis was done for the method using the first 60 stimuli of the full set of 100 stimuli). This type of analysis was used as it negates the considerable differences in the same measurement in different individuals. Because the variance of the difference between 2 measurements is twice the variance of the individual measurements, the standard deviation of the differences must be divided by $\sqrt{2}$ to obtain an estimate of imprecision.

5.2.3. Results

The results for %Repeater F-wave values for individual test hands in the 2 groups are listed in Tables 21 and 22.

DAMAGED MEDIAN NERVES

The first 30 stimuli vs the first 100 stimuli. A paired t-test showed a highly significant statistical difference between the means of the 2 measurements ($p<<0.0001$). The 95% confidence interval for the bias was -7 to -13.1. The imprecision of the method was 10.9.

TABLE 21

COMPUTATION OF THE %REPEATER F-WAVE VALUE USING 30, 60 and 100 STIMULI

%REPEATER F-WAVE VALUES FROM 100 DAMAGED MEDIAN NERVES: MOTOR NEURONE DISEASE AND CARPAL TUNNEL SYNDROME

Test Nerve/Muscle No.	No. of Observations 30	60	100
1.	66	80	100
2.	35	38	52
3.	72	67	70
4.	39	44	61
5.	56	66	55
6.	15	24	39
7.	45	52	70
8.	87	85	86
9.	7	15	32
10.	100	100	100
11.	43	46	50
12.	27	34	51
13.	37	41	52
14.	57	62	64
15.	50	45	65
16.	100	78	71
17.	20	24	42
18.	37	34	40
19.	81	76	83
20.	100	100	100
21.	12	17	30
22.	33	26	50
23.	37	29	47
24.	80	85	89
25.	23	11	36
26.	33	63	67
27.	75	55	75
28.	86	95	88
29.	63	80	84
30.	11	29	37
31.	90	60	62
32.	15	33	42
33.	100	91	89
34.	74	71	68
35.	100	100	100
36.	79	82	76
37.	43	55	55
38.	29	47	62
39.	38	37	40
40.	38	58	62
41.	60	55	39
42.	25	26	41

Test Nerve/Muscle No.	No. of Observations 30	60	100
43.	55	39	38
44.	47	49	62
45.	32	39	57
46.	39	42	33
47.	36	33	55
48.	9	42	43
49.	40	51	57
50.	7	29	38
51.	56	68	57
52.	18	35	40
53.	95	97	89
54.	74	53	52
55.	27	28	46
56.	7	16	31
57.	23	45	53
58.	36	57	61
59.	28	43	41
60.	73	75	77
61.	50	65	88
62.	43	59	80
63.	23	30	46
64.	33	39	50
65.	27	33	41
66.	32	40	52
67.	69	60	58
68.	53	58	60
69.	48	42	42
70.	100	100	100
71.	46	44	47
72.	51	44	50
73.	44	56	55
74.	25	41	45
75.	90	86	89
76.	93	93	82
77.	100	100	100
78.	12	31	42
79.	32	40	50
80.	0	28	54
81.	39	50	56
82.	60	47	50
83.	32	57	64
84.	75	77	86
85.	33	25	40
86.	46	46	47
87.	63	51	46
88.	48	55	65
89.	84	85	87
90.	100	100	100
91.	100	100	100
92.	63	66	75
93.	50	68	71

Test Nerve/Muscle No.	No. of Observations 30	60	100
94.	100	93	82
95.	33	30	45
96.	29	40	44
97.	38	18	37
98.	37	31	38
99.	36	38	39
100.	25	23	33

TABLE 22

COMPUTATION OF THE %REPEATER F-WAVE VALUE USING 30, 60 and 100 STIMULI

MEDIAN NERVE/ABDUCTOR POLLICIS BREVIS: %REPEATER F-WAVE VALUES FROM 124 ASYMPTOMATIC VOLUNTEERS

Test Nerve/Muscle No.	No. of Observations 30	60	100
1.	25	15	12
2.	0	0	0
3.	9	23	28
4.	0	0	0
5.	7	17	23
6.	10	9	13
7.	30	34	27
8.	0	4	10
9.	0	4	14
10.	7	13	10
11.	7	7	4
12.	17	13	21
13.	23	27	22
14.	0	10	9
15.	7	7	6
16.	0	0	4
17.	0	3	5
18.	0	3	4
19.	8	14	23
20.	0	3	6
21.	12	7	10
22.	7	15	14
23.	20	26	20
24.	20	15	20
25.	23	31	25
26.	6	8	7
27.	7	3	4
28.	14	13	24
29.	19	35	27
30.	0	18	13
31.	0	3	10
32.	6	4	9
33.	21	13	18
34.	14	13	16
35.	7	3	3
36.	7	12	16
37.	7	18	17
38.	10	5	11
39.	27	25	25
40.	7	5	6
41.	15	26	23
42.	0	4	18
43.	10	5	7
44.	0	0	4

Test Nerve/Muscle No.	No. of Observations 30	60	100
45.	19	16	20
46.	8	4	6
47.	23	18	20
48.	7	10	8
49.	10	12	15
50.	7	4	6
51.	28	21	13
52.	7	11	11
53.	27	22	21
54.	13	18	16
55.	6	7	12
56.	14	13	19
57.	18	22	17
58.	7	5	4
59.	18	15	22
60.	9	9	9
61.	25	20	22
62.	0	0	0
63.	27	34	60
64.	17	20	22
65.	7	4	5
66.	7	3	4
67.	20	27	27
68.	7	10	16
69.	7	7	15
70.	0	4	5
71.	17	9	16
72.	0	0	11
73.	33	37	31
74.	0	7	10
75.	13	8	11
76.	21	26	28
77.	15	16	19
78.	0	0	6
79.	20	23	22
80.	16	8	4
81.	7	7	6
82.	19	24	32
83.	33	48	48
84.	18	11	11
85.	17	19	14
86.	8	4	7
87.	0	11	20
88.	33	33	34
89.	0	0	0
90.	37	32	28
91.	18	15	9
92.	7	7	13
93.	14	11	16
94.	7	9	8
95.	37	20	24

Test Nerve/Muscle No.	No. of Observations 30	60	100
96.	7	10	10
97.	35	38	41
98.	27	17	31
99.	9	21	21
100.	0	7	4
101.	8	7	7
102.	7	7	6
103.	40	42	42
104.	25	17	20
105.	7	7	9
106.	7	10	13
107.	24	20	17
108.	17	20	27
109.	36	41	34
110.	0	0	6
111.	26	25	24
112.	30	30	37
113.	14	9	10
114.	40	55	50
115.	25	27	38
116.	10	21	29
117.	7	4	8
118.	19	19	13
119.	0	7	8
120.	7	7	10
121.	20	13	18
122.	7	7	9
123.	31	32	35
124.	7	5	8

The first 60 stimuli vs the first 100 stimuli. A paired t-test again showed a statistically significant difference between the means of the 2 measurements ($p<<0.0001$). The 95% confidence interval for the bias was -4.6 to -8.2. The imprecision of the method was estimated at 6.5.

"HEALTHY" MEDIAN NERVES

The first 30 stimuli vs the first 100 stimuli. A paired t-test showed, again, a statistically significant difference between the means of the 2 measurements ($p<0.0001$). The 95% confidence interval for the bias was -1.7 to -4.2. The imprecision of the method was estimated at 5.1.

The first 60 stimuli vs the first 100 stimuli. A paired t-test showed a statistically significant difference between the means of the 2 measurements ($p<0.0001$). The 95% confidence interval for the bias was -1 to -2.8. The imprecision of the method was estimated at 3.6.

(These relative bias and imprecision figures are absolute values and represent %Repeater F-wave values on the 0 - 100% scale).

5.2.4. Comments and Conclusions

In both groups of test nerves/muscles highly significant statistical differences were found in the measurements of the %Repeater F-wave values calculated from the first 30, or the first 60 F-wave sweeps compared with the first 100. The calculation of bias has been made with the understanding that the %Repeater F-wave measurement computed from the first 100 stimuli applied to a test nerve/muscle is an arbitrary, but reasonable, "true" value. The estimations of bias applied to the measurements resulting from

the use of 30 or 60 stimuli are, therefore, more correctly, estimations of relative bias.

The statistical analysis of these data becomes complicated as comparisons are being made between measurements which have values in common, e.g. when the measurement of the %Repeater F-wave value using 60 stimuli is compared with that using 100 stimuli, the latter incorporates the former.

The relative bias associated with both methods under scrutiny (methods using 30 and 60 stimuli rather than 100 stimuli) indicates that the use of smaller numbers of stimuli provides an "underestimate" of the arbitrary "true" value obtained from a method which uses 100 stimuli. The reason for the measured relative bias is noteworthy. In the damaged nerve group, the final 70 F-wave sweeps yielded a higher Repeater F-wave count per number of obtained F-waves than the first 30 sweeps in 70% of test hands. In healthy hands the figure was 61%. It is obvious that the %Repeater F-wave value calculated from the first 30 compared with the last 70 F-wave sweeps is statistically different in both groups (hence the bias). The consistently smaller value obtained from the earlier (e.g. 30) compared with the later stimuli shows that the test itself (the method) is affecting the measurement. The same relative bias is present when the first 60 of the first 100 F-wave sweeps are used to compute the %Repeater F-wave value indicating that the F-discharge pattern is significantly different in the period when the last 40 stimuli are applied compared with the period when the first 60 stimuli are applied. The bias (in both groups) is less when the first 60 rather than the first 30 stimuli of the full 100 are used to calculate the %Repeater F-wave value. This may be due, at least in part, to the incorporation of results from the second 30 stimuli into both the 60 and 100 stimuli paradigm.

In general terms, the longer the test goes on the more Repeater F-waves there are as a percentage of the obtained F-responses.

Why the application of supramaximal stimuli at 1 Hz should be associated with a change in F-response pattern is not obvious. The author is not aware of a previous report suggesting this phenomenon.

The magnitude of the relative bias is such that the application of a 30 or 60 stimuli method to a damaged median nerve would be associated with a clinically significant difference in the measurement of the %Repeater F-wave value when compared with the method using 100 stimuli.

The estimate of imprecision of the method using 30 and 60 stimuli shows that imprecision of both methods is significant. The imprecision lessens when the number of test stimuli increases. The greatest imprecision was found when only 30 stimuli were used to calculate the %Repeater F-wave value in the damaged nerves. This could be anticipated when one considers the variably impersistent F-discharge patterns containing small numbers of individual F-wave types. For example, if only 10 F-responses are recorded from 100 stimuli, but 8 identical F-responses occur with the last 10 stimuli, and 2 different individual F-waves (not Repeater F-waves) are seen in the first 30 F-wave sweeps, the %Repeater F-wave value would be 80% calculated from the 100 stimuli method and 0% calculated from the 30 stimulus method.

When the method of obtaining the %Repeater F-wave value using 30 stimuli is compared with the method using 100 stimuli, bias is high and imprecision is high. Both are lessened but remain statistically significant when the number of test stimuli is increased from 30 to 60. The relative bias which has been identified in association with the use of the initial 30 or 60 F-wave sweeps is related to the technique applied to the patient. In view of the high relative bias and relatively higher imprecision associated with brief

stimulus trains, the use of longer trains, such as 100, are recommended to calculate the %Repeater F-wave value. The reduction in the imprecision of the method and the effect of the later stimuli in the test stimulus train on the test motor/neurone pool are both advantageous to the accurate and sensitive identification of abnormalities of the F-discharge pattern in a test adductor pollicis brevis motor neurone pool. The use of small trains of stimuli (e.g. 30) is associated with at least 2 obvious drawbacks.

5.3. Altered F-wave Generator Activity as an Isolated Electrodiagnostic Sign of Peripheral Nerve Dysfunction: An Experiment

5.3.1. Introduction

The difficulties which, not uncommonly, arise in correlating electrophysiological abnormalities with an individual patient's neurological symptoms will be illustrated in 6.7. The author has encountered several patients with symptoms typical of carpal tunnel syndrome who have had no electrophysiological abnormality on conventional nerve conduction studies, but whose abductor pollicis brevis %Repeater F-wave value has been outwith the reference range (see 5.4), and whose follow-up examination revealed the evolution of conventional nerve conduction study abnormalities. This observation suggested that, in some cases, abnormalities of backfired "late" motor responses may precede any other identifiable nerve conduction abnormality in peripheral nerve entrapment.

This experiment is concerned with the sensitivity of spinal F-wave generators to peripheral nerve compression and follows from those initial observations which suggested that a pathological pattern of alpha motor neurone backfiring might be an isolated electrodiagnostic sign. Additionally, the experiment was devised to determine if an abnormal %Repeater F-wave value, found as an isolated electrodiagnostic sign, can be expected to occur with a high or low prevalence in routine electrodiagnosis.

For this purpose it was necessary to find a group of subjects who were at high risk of having a subclinical peripheral nerve lesion. The liability to develop carpal tunnel syndrome is linked to the genetically determined volume of the carpal tunnel and many patients have symptoms of median entrapment bilaterally (Dekel and Coates 1979). It is a common finding in patients with unilateral symptoms of carpal tunnel syndrome that there are

electrophysiological abnormalities of the opposite median nerve which have no clinical correlate. The asymptomatic contralateral median nerves in patients with unilateral symptomatic carpal tunnel syndrome were therefore used to assess the prevalence of pathological %Repeater F-wave values in asymptomatic nerves judged to be at risk of entrapment. In the same group of nerves the prevalence of sensory fibre dysfunction was also established.

5.3.2. Methods and materials

Seventy-seven patients with unilateral symptomatic carpal tunnel syndrome were studied. Their ages ranged from 34 to 78 years (mean 45 years). Forty-five were female and 32 were male. Four suffered from maturity onset diabetes mellitus and 3 from rheumatoid arthritis. The rest suffered "idiopathic" carpal tunnel syndrome.

The electrodiagnosis of median nerve dysfunction at the carpal tunnel level was made using conventional nerve conduction studies (sensory, motor (including F-wave latency parameters) and "mixed" nerve conduction were evaluated) and electromyography applied to the symptomatic limb. Each case had at least one of the following parameters outwith this laboratory's normal range: sensory antidromic wrist-palm latency (see 6.5) (Kimura 1979), median nerve palm-wrist "mixed" nerve conduction velocity, minimum median F-wave latency (> minimum ulnar F-wave latency by $\geq$2.3 ms (mean + 2 SD.)) (evoked just proximal to the distal crease of the wrist), and/or denervation potentials detected in abductor pollicis brevis, but not in abductor digiti minimi or the first dorsal interosseous muscle.

The asymptomatic contralateral limb was examined for signs of radiculopathy, myelopathy and peripheral nerve entrapment. No signs were found in any of the limbs included in the study.

Having confirmed the lesion at carpal tunnel level on the symptomatic side, each contralateral asymptomatic median nerve was subjected to the following protocol: the distal motor latency, the sensory antidromic wrist-palm latency, (over 8 cm) (Kimura 1979) and the %Repeater F-wave value from abductor pollicis brevis (stimulating the median nerve just proximal to the proximal edge of the transverse carpal ligament) were calculated. To determine the %Repeater F-wave value 100 F-wave sweeps were recorded. The methodology and equipment used were identical to that described in 2.2 and will not be reiterated. The method of calculating the %Repeater F-wave value is described in 2.3. In those nerves in which the %Repeater F-wave value was abnormal but the sensory antidromic wrist-palm latency and distal motor latency fell within normal limits ($\leq$1.7 ms, <4 ms respectively) two further measurements were obtained: the minimal F-wave latency for the median and ipsilateral ulnar nerve (recording the latter from the motor point of abductor digiti minimi, stimulating the ulnar nerve just proximal to the wrist) using 20 stimuli at each site. The reference range for abductor pollicis brevis' %Repeater F-wave values is contained in 6.5 (Table 24, Figure 35). Except for 3 patients, the %Repeater F-wave values for these subjects in this experiment came from patients who were $\leq$65 years of age; the control reference range from asymptomatic volunteers of 26-65 years was therefore used to establish whether the patients %Repeater F-wave values were likely or unlikely to be pathological.

5.3.3. Results

%Repeater F-wave values, sensory antidromic wrist-palm latencies and minimum F-wave latency data are listed in Table 23 on pages 246 and 247.

TABLE 23

ASYMPTOMATIC MEDIAN NERVES AT RISK OF ENTRAPMENT: ELECTROPHYSIOLOGICAL PARAMETERS

Nerve No.	%Repeater F-wave Values (%)	Sensory Antidromic Wrist-palm Latency (ms)	Latency Difference between Wrist Evoked Ipsilateral Ulnar and Median Minimal F-wave Latencies (ms)
1	61	1.5	1.9
2	47	1.5	1.5
3	49	1.4	2.0
4	83	1.6	3.4
5	52	1.7	2.2
6	62	1.6	1.8
7	57	1.6	2.2
8	54	1.5	1.9
9	66	1.6	2.1
10	82	1.4	3.2
11	67	1.3	2.0
12	48	1.6	1.8
13	53	2.8	
14	49	2.5	
15	66	2.1	
16	78	2.0	
17	54	2.1	
18	58	2.5	
19	61	3.0	
20	53	1.9	
21	87	2.6	
22	94	2.4	
23	18	2.3	
24	28	2.1	
25	5	1.9	
26	6	2.0	
27	11	2.5	
28	27	2.3	
29	4	1.4	
30	0	1.6	
31	5	1.5	
32	2	1.4	
33	9	1.5	
34	0.	1.6	
35	6	1.6	
36	7	1.6	
37	18	1.5	
38	13	1.7	
39	0	1.6	
40	4	1.4	
41	3	1.4	
42	5	1.6	

Nerve No.	%Repeater F-wave Values	Sensory Antidromic Wrist-palm Latency	Latency Difference between Wrist Evoked Ipsilateral Ulnar and Median Minimal F-wave Latencies
43	2	1.5	
44	10	1.6	
45	6	1.4	
46	12	1.3	
47	0	1.2	
48	0	1.7	
49	9	1.6	
50	12	1.3	
51	7	1.7	
52	15	1.2	
53	9	1.4	
54	13	1.4	
55	4	1.5	
56	5	1.7	
57	0	1.6	
58	11	1.6	
59	18	1.6	
60	9	1.5	
61	27	1.6	
62	9	1.5	
63	17	1.5	
64	31	1.5	
65	0	1.4	
66	6	1.7	
67	8	1.7	
68	12	1.3	
69	0	1.3	
70	10	1.6	
71	9	1.6	
72	4	1.5	
73	2	1.5	
74	7	1.6	
75	29	1.6	
76	14	1.6	
77	3	1.6	

Thirty-six per cent of the asymptomatic nerves tested were found to have an electrophysiological abnormality. Twenty-eight nerves were found to have a sensory antidromic wrist-palm latency >1.7 ms and/or a %Repeater F-wave value above the 95 percentile value of the control range (34%). In six nerves a sensory fibre abnormality was the only electrodiagnostic abnormality found and in 12 nerves a pathological %Repeater F-wave value was the only abnormality detected. Ten of the 77 nerves had abnormal %Repeater F-wave values and abnormal sensory wrist-palm latencies, of which three had prolonged distal motor latencies. Of the 12 nerves which gave normal sensory fibre values but whose %Repeater F-wave values were high, 10 had minimal median F-latency values within 2.3 ms of the minimal ulnar F-wave latency value.

Of the asymptomatic nerves in which an electrophysiological abnormality was found, 10 out of 28 (36%) were detected through the use of the %Repeater F-wave value alone.

5.3.4. Comments and conclusion

The choice of the contralateral asymptomatic median nerve in patients with unilateral symptomatic carpal tunnel syndrome proved suitable for the purposes of this study as isolated F-discharge abnormalities were found in 36% of hands tested. Of the 28 nerves in which a subclinical lesion was identified electrodiagnostically, 10 had an abnormality of F-discharge patterns as an isolated electrodiagnostic sign. This finding suggests that by quantifying the backfired responses of the motor neurone pool of abductor pollicis brevis a lesion of the median nerve can be detected which could go undetected by conventional nerve conduction study methods. The ascription of a subclinical lesion to the test nerve in which an isolated %Repeater F-wave abnormality is found is, of course, assumptive. However, the findings

in these test nerves tend to support the observation that, with asymptomatic median nerve compression, F-wave discharge patterns can be modified before conventional nerve conduction study parameters become abnormal.

An abnormal %Repeater F-wave value obtained from a single stimulus site in the median nerve does not, of course, localise the lesion to the carpal tunnel. The %Repeater F-wave values calculated from a single site provide data which has to be interpreted in the light of the clinical and associated neurophysiological/neuroradiological features. A technique to detect and localise median nerve dysfunction within the carpal tunnel, using the %Repeater F-wave measurement, will be presented in 6.6.

5.4. Surgical Decompression for Peripheral Nerve Entrapment when the Only Electrodiagnostic Abnormality is a Pathological %Repeater F-wave value

5.4.1. Introduction

A number of patients referred to the author for electrodiagnostic confirmation of carpal tunnel syndrome or investigation of non-specific pain and sensory syndromes of the arm and/or hand have been found to have isolated abnormalities of F-wave discharge patterns. In some instances the author believes that this finding has been of help in deciding the treatment in individual patients. An illustrative example will be provided.

5.4.2. Case report

A, O'R - (Tayside Health Board Number 05 10 25): Since February of 1984 the patient, then 59, had been troubled by persisting nuchalgia associated with pain, numbness and paraesthesiae in the left upper limb. He had been treated in a number of different ways. The use of a cervical collar, intermittent neck traction and several courses of physiotherapy had proved unhelpful. Fourteen months later he was referred from the orthopaedic clinic, Dundee Royal Infirmary, to that hospital's Department of Neurosurgery, with a diagnosis of cervical radiculopathy. As the patient was thought to have a reduction in amplitude of the left biceps reflex associated with sensory disturbance on the radial side of the hand it was felt that spondylotic damage was occurring primarily at the C6 root level.

On 22/4/85 a posterior cervical "decompression" was performed on the left C5/6/7 roots. The operation note describes how the C6 foramen was not compressed and how "this was disconcerting in view of the patient's symptoms". The C7 foramen was compromised by a significant anterior

osteophyte which was "widely decompressed".

Post-operatively, there was an improvement in the patient's nuchalgia but other symptoms in the upper limb persisted. He complained bitterly of weakness in his hand, for pinch in particular, sensory disturbance (particularly in the radial side of the hand) and pain over the wrist and forearm. At this stage he was referred to the author for further evaluation.

It was found that his sensory symptoms could be reproduced by forced flexion of the wrist and the arm reflexes were then symmetrical and normal. Conventional nerve conduction studies showed no signs of median nerve dysfunction. The sensory antidromic wrist-palm latency (Kimura 1979) was 1.5 msec and the distal motor latency was 3.6 msec. F-wave latency studies showed no abnormality. The only electrodiagnostic clue to dysfunction in the median nerve was a high %Repeater F-wave value of 52% (for control range see 6.5, page 285). In view of the isolated F-wave abnormality, coupled with the isolated clinical sign it was felt that he probably had an atypical carpal tunnel syndrome. The patient understood that the diagnosis of median entrapment was by no means certain and, with his understanding of this, the left carpal tunnel was decompressed on 4/3/86. The median nerve was found to be "grossly flattened at the level of the transverse carpal ligament" (operation note). One week post-operatively, when he was seen for review at the orthopaedic clinic, there was a marked improvement "in sensation and symptoms of the 2nd and 3rd digits of the left hand" (clinic note). The thumb took 7 weeks to recover to normal. The author has since reviewed the patient in October of 1987 when he was asymptomatic. At this stage the %Repeater F-wave value had returned to a normal level at 22%.

5.4.3. Comment

The patient's signs and symptoms were interpreted, by both orthopaedic and neurosurgical specialists, as originating from the cervical canal. The operative intervention at neck level had no significant impact on his arm and hand symnptoms which were promptly relieved by carpal tunnel decompression (note they had been present and unrelenting since Feburary 1984). The only electrodiagnostic abnormality which pointed to an alternative lesion was the F-wave discharge pattern through the C8,T1 neurones of abductor pollicis brevis. It is of interest that such disabling pain and sensory symptoms were not associated with conventional sensory and motor parameter abnormalities, particularly in view of the duration of the symptoms and the macroscopic appearance of the median nerve at operation. ("False-negative" electrodiagnostic tests will be considered in Chapter 6). The %Repeater F-wave abnormality obtained from a single stimulus site does not, of course, localise the lesion along the length of the lower motor neurones under test, but in this instance did focus attention on motor fibres through a different segmental level than that which had been suspected as a source of symptoms. Localisation of dysfunction to the carpal tunnel was, in this instance, prompted by the reproduction of the patient's sensory symptoms with forced flexion of the wrist. The author finds that isolated F-wave abnormalities (of F-latency and of %Repeater F-wave values) can be extremely helpful in the context of a patient's symptoms, and regards the electrodiagnostic evaluation as an extension of the clinical examination.

The place of the F-wave in "distinguishing" between atypical carpal tunnel syndrome and cervical spondylosis will be considered in detail in 6.7.

The author has referred a number of other patients who have had both classical and atypical carpal tunnel synptoms for surgery on the basis of %Repeater F-wave abnormalities alone (some with a good outcome). This

case report is included, merely to illustrate that the F-discharge pattern may, possibly, have a place in the practical management of patients with hand/arm/neck symptoms. Other cases (anecdotes) will not be described as there are considerable difficulties attached to interpreting the response to surgery of such patients (even the macroscopic appearance as described by the surgeon at operation is hard to interpret with respect to the symptoms).

Very large numbers of this type of case would need to be assessed post-operatively before a meaningful conclusion could be drawn on the use of this test in this type of patient (i.e. sole electrodiagnostic abnormality in patient with non-specific symptoms). The spontaneous remission rate in carpal tunnel syndrome is Ca. 30% (Muhlau 1984), a factor which makes measurement of therapy extremely difficult. However, the author believes that this should ultimately be studied experimentally.

The cited case provides a number of clues highly suggestive, in this instance, that the subtle electrodiagnostic abnormality in the median nerve was relevant to the symptoms and their response to decompression of the carpal tunnel.

CHAPTER 6

CHAPTER 6

THE F-WAVE IN THE ELECTRODIAGNOSIS OF MEDIAN NERVE DYSFUNCTION IN THE CARPAL TUNNEL

6.1 Introduction

Carpal tunnel syndrome is the commonest peripheral nerve entrapment syndrome seen in most EMG laboratories (Editorial, Lancet 1985). The electrophysiological evaluation of patients with a clinical diagnosis of carpal tunnel syndrome and patients whose symptoms might represent median nerve dysfunction takes up a large fraction of the schedule of the EMG laboratory in which the author works. The interpretation put on these electrodiagnostic results has considerable practical relevance to the way in which such patients are managed. When symptoms and signs are typical of median nerve dysfunction and electrophysiological abnormalities are clear cut, correlation of the two poses no difficulty (and there are good reasons for making pre-operative electrophysiological measurements in patients with clear cut carpal tunnel syndrome). However, patients with non-specific symptoms and marginal electrodiagnostic abnormalities or patients with non-specific symptoms lacking any electrodiagnostic abnormality pose difficulties. These difficulties, which recur fairly frequently, and the place of the F-wave in both solving and generating diagnostic and interpretive problems will be considered.

The lack of a description of Paralysis Agitans in the writings of physicians from ancient cultures, e.g. Greece and Persia, has been used to suggest that the disease is a disorder of post-industrial times. While this may indeed prove to be an important epidemiological clue, carpal tunnel

syndrome is another example of a common neurological disorder which was not well recognised until recent times.

Phalen reported 11 cases of carpal tunnel syndrome to the American Medical Association in 1950 and it was only then, surprisingly, that a general awareness of that syndrome began to develop (although Marie and Foix had described the condition in 1913) (Phalen 1951). The electrodiagnosis of carpal tunnel syndrome was reported in 1956 by Simpson and for many years estimation of the median nerve's distal motor latency was the customary measurement in most EMG laboratories for the detection of median nerve entrapment under the flexor retinaculum. Another major advance in the electrodiagnosis of carpal tunnel syndrome was the recording of sensory nerve action potentials (Dawson and Scott 1949, Gilliatt and Sears 1958). Human nerve action potentials had first been recorded by Eichler in Freiburg in 1937. In the late 1940's Dawson and Scott (1949) suggested that "the recording of nerve action potentials may be a delicate means of detecting minor degrees of damage". The electrical stimulation of digital fibres had been used to study the conduction velocities of sensory fibres in the median and ulnar nerves around the same time that the distal motor latency measurement was devised (Dawson 1956).

Despite further advances in clinical neurophysiology, (see below), a widespread belief was held that median entrapment could be readily, and accurately, diagnosed from a history of the symptoms and a detailed physical examination (Phalen 1970). This view is still encountered quite frequently, in the author's experience. The textbook description of the patient wakened in the night by hand pain and numbness, dangling the hand over the edge of the bed to obtain relief is not one which the author has met very frequently. While nocturnal symptomatology is an extremely helpful clue to carpal tunnel syndrome, the spontaneous description of a "flick sign"

is diagnostically much more useful and is given by the majority of patients who experience numb waking.

The prevalence of key diagnostic features such as, a positive wrist flexion test, Tinel's sign or prolongation of the distal motor latency is low in the patients diagnosed as suffering from electrodiagnostically verified carpal tunnel syndrome in this laboratory (Macleod 1987). This reflects the general trend over the past 15 years, or so, towards earlier diagnosis of median nerve dysfunction and, in particular, identification of the lesion prior to the onset of thenar muscle wasting (Eklund 1975, Kimura 1979, Mills 1985). Sensitive electrophysiological tests also allow identification of median nerve lesions which are not associated with classical clinical features. The interpretive problems (relating to both symptoms and electrophysiological findings) arising from this will be highlighted later. The sensitivity of these more recently introduced electrodiagnostic tests has not only allowed the diagnosis of median nerve dysfunction at an early stage but has also gone some way to redefine the clinical syndrome of median nerve entrapment at the wrist, so called carpal tunnel syndrome.

The yield of electrodiagnostic median nerve abnormalities in suspected cases of carpal tunnel syndrome has been significantly increased through the use of techniques which measure impulse transmission across the damaged segment of the nerve selectively (Eklund 1975, Kimura 1979, Mills 1985). Roth (1970) first described a method for studying motor fibres as they pass under the transverse carpal ligament in which axons are stimulated, to activate the thenar muscles, first at the wrist and then in the palm of the hand. Buchtal and, later, Daube showed, with studies of orthodromic sensory conduction, that electrophysiological median nerve abnormalities in carpal tunnel syndrome were often limited to the length of nerve in the carpal tunnel (Buchtal et al 1974, Daube 1977). Using these techniques, sensory or

motor fibre conduction can be measured across the length of the carpal tunnel. Kimura took the trans-tunnel evaluation of the median nerve a stage further and showed, using an "inching" technique, that dysfunction could be further localised to a 1 cm length of nerve, most frequently at the distal edge of the transverse carpal ligament (Kimura 1979) (see Figure 30).

The value of having a very sensitive test with a low false-negative detection rate is evident in patients with conditions such as severe rheumatoid arthritis, multiple sclerosis and cervical spondylosis in whom carpal tunnel syndrome is also present (in two, rheumatoid arthritis and cervical spondylosis, their presence is a risk factor for developing carpal tunnel syndrome (Upton and McComas 1973)). These conditions and carpal tunnel are all capable of producing pain, dysaesthesiae, muscle weakness or muscle wasting in the same anatomical distribution. The physical signs and symptoms in that setting are, necessarily, difficult to interpret and it can be impossible to diagnose a median nerve lesion definitively without recourse to nerve conduction studies and electromyography. On the other hand, the high sensitivity of these tests also allows the detection of clinically irrelevant nerve lesions and this introduces unwanted complexity into the matching of clinical and electrodiagnostic findings. An example of an incidental electrodiagnostic abnormality is provided by median nerve dysfunction which is frequently present in the contralateral asymptomatic wrist of patients who present with unilateral symptomatic carpal tunnel syndrome (see 5.3). Pathological focal median nerve lesions have been found with a high prevalence in asymptomatic hands at post-mortem (Neary et al 1975). The author finds that Phalen's test is of particular use when an electro-physiological abnormality of the median nerve is detected in a patient whose symptoms are atypical of median nerve compression; if forced flexion of the wrist reproduces these non-specific or atypical symptoms perfectly, then it is

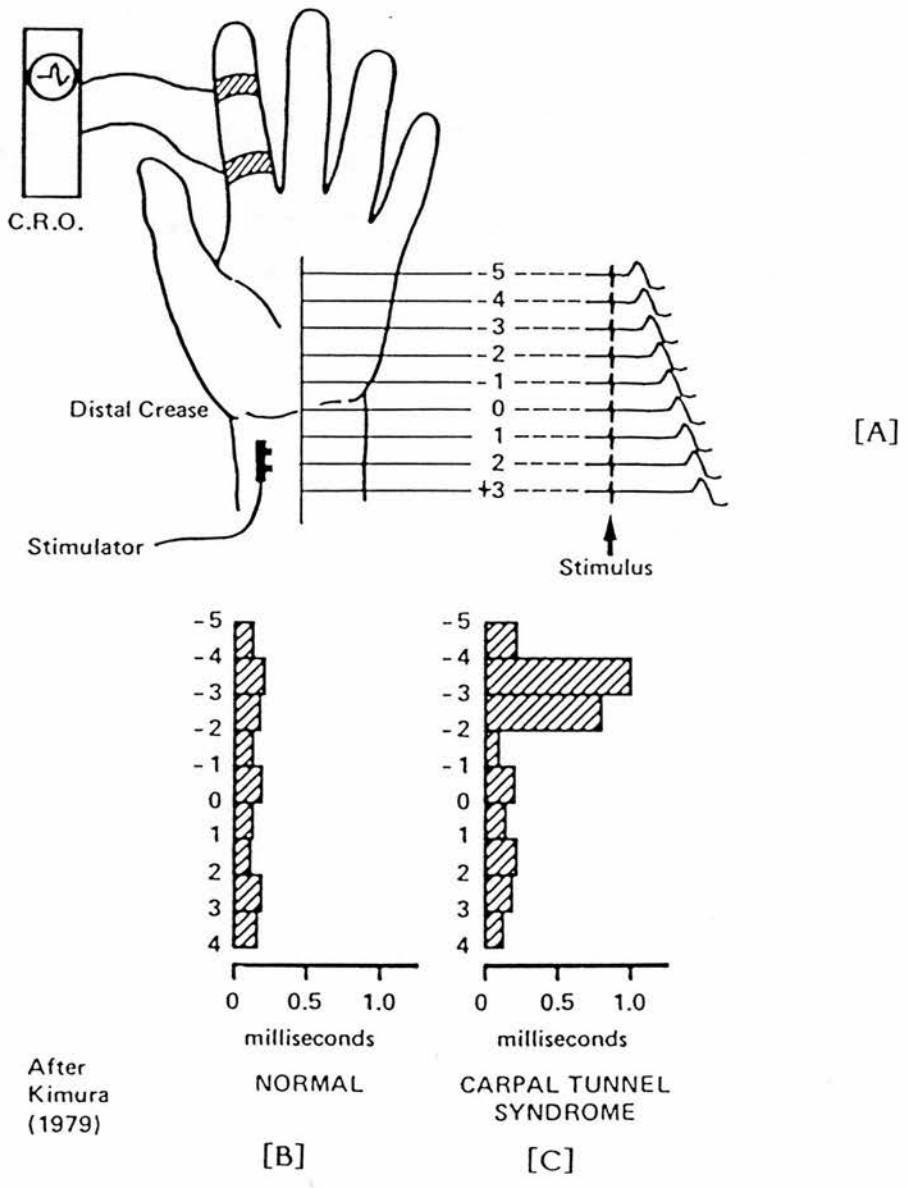


FIGURE 30

KIMURA'S "INCHING" TECHNIQUE FOR DETECTING SENSORY FIBRE LESIONS IN THE MEDIAN NERVE UNDER THE FLEXOR RETINACULUM

The O point is at the distal skin crease of the wrist.

[A] shows the normal graded increments in latency of the SAP obtained by moving the stimulating cathode in 1 cm steps along the wrist-palm segment.
[B] & [C] show the normal and pathological latency increments which can be detected across 1 cm segments of the median nerve in the carpal tunnel in health and in carpal tunnel syndrome respectively.

SAP = sensory action potential.

more likely that nerve fibre dysfunction localised to the carpal tunnel segment is of relevance to the symptomatology.

In contrast, "false-negative" electrodiagnostic tests are occasionally a problem. The fraction of patients with a putative diagnosis of carpal tunnel syndrome found to have an electrodiagnostic abnormality of the median nerve has increased in recent years and the "false-negative" rate has fallen. In some instances one might assume that entrapment of a peripheral nerve may cause symptoms without producing nerve fibre dysfunction. (The author has seen a number of patients with typical symptoms of median nerve compression who had no abnormalities on their initial nerve conduction study, but on re-testing, some weeks later, electrodiagnostic abnormalities had evolved. The author has also encountered a number of patients with typical symptoms which have been of very long standing (up to 10 years) and even in the presence of such long unremitting complaints typical of carpal tunnel syndrome, the electrodiagnostic tests have shown no abnormality). In other cases selective nerve fibre damage can affect one type of fibre and spare another type, e.g. sensory fibres may be damaged and motor fibres remain intact. Conventional electrodiagnostic tests often show partial sparing in the cutaneous territory of the median nerve when an abnormality may be found in the territory of only a single digital nerve. (It is, of course, a common clinical finding that hypalgesia is detectable in only a small zone of the nerve's cutaneous territory). However, if the electrophysiological tests, which are currently used, do fail to detect the presence of nerve damage in some instances (a true "false-negative" test), any additional means of examining nerve fibre function in the carpal tunnel would be valuable.

In this chapter the current utilisation of the F-response in the detection and localisation of median nerve lesions will be reviewed and a number of experiments will then be detailed. These are concerned with extending the use of the F-response in the detection of median nerve lesions. Two new methods will be described. The other main concern of this chapter is the difficulty in making a correct clinical differentiation between carpal tunnel syndrome and cervical spondylosis. The role which the F-response plays in helping differentiate the two will be discussed. A new clinical sign, originated by the author, relating to the diagnosis of carpal tunnel syndrome clinically will also be described.

6.2 F-wave Measurements in Carpal Tunnel Syndrome

Sunderland (1968) found that motor fibres were especially sensitive in experimental tourniquet induced nerve lesions. They often failed first, and in mild lesions they could be the only fibre type to suffer. Kimura confirmed that in carpal tunnel syndrome motor fibres could be selectively affected under the transverse carpal ligament while sensory conduction measurements remained normal (Kimura 1979). In day to day practice the reverse is also seen. Sensory and motor fibre tests are therefore complimentary in the electrophysiological assessment of median nerve function. The sensitivity of the F-response in detecting nerve fibre lesions was hinted at by observations contained in the original paper on the F-wave (Magladery and McDougal 1950). It was found that F-waves elicited by stimuli delivered distal to a pressure cuff on the nerve were progressively delayed by several milliseconds at a time early in the experiment when no increase in M wave latency was observed if the stimulus was placed proximal to the cuff. Sensitive tests of motor fibre function are important as they may allow definition of a nerve lesion in advance of Wallerian degeneration and in the absence of any identifiable sensory fibre dysfunction. Within the past 10 years an important application for the F-wave has been the detection of median nerve lesions in the carpal tunnel. It is noteworthy that, as recently as 1979, the use of the F-response in detecting median entrapments was not cited in a review by Kimura (Kimura 1979). There are still EMG laboratories with a research interest which, in recent times, have failed to incorporate F-wave latency analysis into their evaluation of patients with putative carpal tunnel syndrome (Halter et al 1980).

To date, the F-wave has been used to provide a sensitive measurement of motor fibre conduction in the assessment of carpal tunnel syndrome (Egloff-Baer et al 1978, Maccabee et al 1980). F-wave latency measurements

provide information on the fastest coducting motor fibres which are the largest and, often, the fibres most vulnerable to compression damage (Gilliatt and Harrison 1984, Shahani et al 1987). F-wave latency measurements are very much more sensitive than measurement of the distal motor latency in the presence of motor fibre lesions and may be the only detectable neurophysiological abnormality (Personal Observations, Egloff-Baer et al 1978). This is of particular importance when the clinical diagnosis is uncertain (for example, if there is uncertainty in the clinician's mind between a median nerve entrapment syndrome and a C6 sensory radiculopathy) and sensory and mixed nerve studies disclose no abnormality of median nerve function. In this context an isolated C8, T1 F-wave latency abnormality can be useful, although the interpretation of such a finding is sometimes arbitrary (see below). The author believes that C6 dermatome sensory symptoms associated with C8, T1 F-wave delay need careful consideration and that, in at least some patients, symptoms can be abolished by surgery to the carpal tunnel (see 5.4/6.7).

There are several ways of maximising the diagnostic sensitivity of F-wave latency measurements. The minimal F-wave latency and F chronodispersion values are obtained by recording from the motor point of abductor pollicis brevis while stimulating the nerve at the wrist. Side to side comparisons of latency values in individual patients can be very useful, as many variables inherent in inter-subject comparisons are eliminated (Kimura 1983, Lachman et al 1980, Peioglou-Harmoussi et al 1985(a)). In healthy subjects the minimal F-wave latency transmitted by the median nerve and recorded from abductor pollicis brevis has been shown to be slightly longer in the right than the left median nerve (Peioglou-Harmoussi et al 1985(a)). (This could, possibly, be related to subclinical entrapment in the dominant limb). In routine use of the F-wave it is important to record a sufficient

number of responses to make it likely that the minimal F-wave latency is measured. Panayiotopolous and colleagues showed, in healthy subjects, that only three (approximately) of 20 consecutive F-responses were conducted along the fastest motor fibres (Panayiotopolous et al 1977). Others have found that recording 20 responses gave only a 59% probability of being within 0.5 msec and a 76% probability of being within 1 ms of the minimum value obtained from at least 100 responses from every test nerve/muscle (Peioglou-Harmoussi et al 1985(a)). From a practical point of view it is not feasible (or always necessary) to record 100 responses from every test/muscle in the course of routine nerve conduction studies. Each test should be individually tailored to suit the circumstance, e.g. the first five F-waves recorded may clearly indicate gross delay or excess F-wave chronodispersion and further recordings would be superfluous.

While helpful in some instances, comparison of F-wave latencies of a symptomatic median nerve with a contralateral asymptomatic median nerve can sometimes be unhelpful as electrophysiological abnormalities are commonplace in the contralateral asymptomatic median nerve of patients with unilateral carpal tunnel syndrome (see 5.3). When this happens the sensitivity of the comparison is reduced.

Just as the median nerve's "mixed" conduction velocity can be usefully compared with the ulnar "mixed" nerve conduction velocity across the wrist-palm segment, comparison of the F-wave latencies of the two nerves in the same limb can be useful. Figure 31 illustrates a case in which a comparison of minimal F-wave latencies obtained from thenar and hypothenar muscles in a symptomatic hand allowed identification of a median nerve motor fibre lesion.

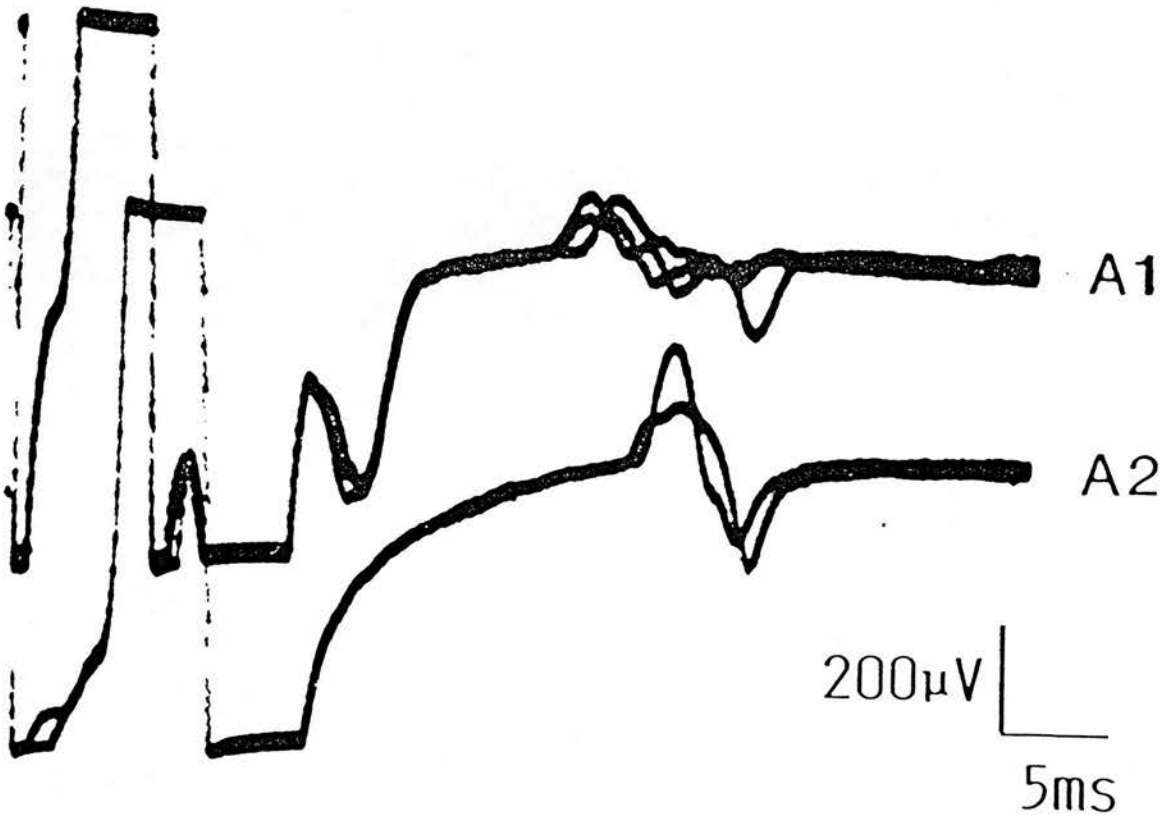


FIGURE 31

COMPARISON OF IPSILATERAL ULNAR AND MEDIAN F-WAVE LATENCIES IN CARPAL TUNNEL SYNDROME

(A1) shows superimposed F-wave sweeps recorded from the hypothenar muscles with a surface electrode stimulating the ulnar nerve just proximal to the distal crease of the wrist. The minimal F-wave latency is 26.2 ms (of a larger series). (A2) shows F-waves recorded in a similar manner from thenar muscles stimulating the median nerve at the wrist. The earliest F-wave appeared at 30.7 ms. The inter-muscle minimal latency F-wave difference is pathological.

In a series of 103 control subjects Egloff-Baer and colleagues (1978) found that the differences in latencies between the F-waves of abductor pollicis brevis and the F-waves of abductor digiti minimi never exceeded 2 ms. In some nerves damaged by entrapment the minimal F-wave latency remains within the normal range while excessive F chronodispersion may be present. (The pathophysiological mechanisms which explain this observation are obscure).

The likelihood of recording maximised F chronodispersion is increased by recording large numbers of responses. Side to side comparison of F-chronodispersion values in an individual can be of use when other tests do not disclose an abnormality. The upper limit control F chronodispersion value for the median nerve, recording from abductor pollicis brevis while stimulating at the wrist, varies in different studies from 2.2 (S.D. 1.1) to 3.6 (S.D. 1.2) (Shahani et al 1980(a), Peioglou-Harmoussi et al 1985(a)).

Prolongation of the F-response transmission time could result from a lesion (or lesions) at any point along the test axons, i.e. in the mixed nerve, the brachial plexus or the ventral roots of C8,T1 (see Chapter 4). Even a lesion affecting the motor neurone pool of abductor pollicis brevis in the spinal cord is capable of delaying the F-wave latencies (Peioglou-Harmoussi et al 1986). Syringomyelia and compression of the median nerve in the carpal tunnel can both present with painless wasting of the thenar eminence (the author has seen the latter only once) and could, theoretically, result in identical F-wave latency abnormalities. F-wave latency measurements, as are conventionally made in most EMG laboratories, are insufficient for the localisation of a median nerve lesion in the carpal tunnel. Isolated abductor pollicis brevis F-wave latency abnormalities can prove difficult or even impossible to interpret in the context of some patients' symptoms, while in other cases they can be very useful in directing attention to a lesion of the

median nerve.

Further localising information may be got if a second set of stimuli is applied at a more proximal site over the median nerve, from which the F-ratio can be calculated. This allows a comparison of motor conduction latencies in the proximal and distal segments of the mixed nerve. (The author is not aware of a published study on the use of the F-ratio in the diagnosis of median nerve entrapment). The measured F-wave conduction velocities in human studies have suggested conduction is faster proximally than it is distally but the F-ratio approaches unity with the stimulus placed at the elbow (Kimura 1974, Kimura and Butzer 1975, King and Ashby 1976 and Ongerboer de Visser et al 1982). In carpal tunnel syndrome the F-ratio may be reduced (Kimura et al 1979). The use of the F-ratio is complicated by the possibility of a double crush phenomenon (Upton and McComas 1973, Eisen et al 1977(a)). If proximal as well as distal slowing is present the ratio may not be reduced sufficiently to be of diagnostic value.

6.3 Localisation of Median Nerve Dysfunction to Carpal Tunnel Level Using F-wave Latency Measurements

Localisation of an F-wave transmission defect to the carpal tunnel segment of the median nerve can be made by stimulating the nerve first at the wrist and then over the thenar branch in the palm of the hand. It has been claimed this technique increases the sensitivity of F-wave latency recordings in the detection of median entrapment in the carpal tunnel compared with the technique using F-wave latencies evoked with the stimulus at the wrist alone (Maccabee et al 1980). If the F-response latencies obtained with a wrist stimulus fall in the normal range, but those evoked by a stimulus distal to the carpal tunnel are delayed, then the site of dysfunction can be placed between the two stimulus sites. This gives a more accurate localisation than the F-ratio which could be reduced by a median nerve lesion in the forearm as well as by lesion in the carpal tunnel. The method is, however, not without potential drawbacks (which were not considered by Maccabee and colleagues (1980)). The minimal F-wave latency value obtained with the palm stimulus may be misleading as F-waves can arise from adductor pollicis by inadvertent stimulation of the ulnar branch to that muscle. Surface electrodes over the motor point of abductor pollicis brevis can record F-responses from the muscle deep to abductor pollicis (see page 295). A false-negative test could result from normally conducted ulnar F-waves being mistaken for responses conducted in the median nerve. This problem could be overcome by using a needle electrode to record the F-responses from abductor pollicis brevis or, alternatively, by using the maximal latency F-response obtained when stimulating in the palm. These techniques have not, so far, been evaluated.

The technique of localising a mixed peripheral nerve lesion by determining the pattern of F-response delays in different muscles in the territory of that nerve will not be discussed here, as it has already been described in 4.1.2). The method is useful and can be applied to the median nerve when a lesion under the ligament of Struthers, a Pronator syndrome, or an anterior interosseous nerve lesion is suspected. Side-to-side comparison of minimum F-wave latencies and/or F chronodispersion in the different muscles of thenar eminence and forearm are particularly useful. An illustrative case is contained in 4.1.2.

6.4. F-wave Amplitude in Carpal Tunnel Syndrome

One might expect F-wave amplitudes to be increased when motor unit territories are expanded by reinnervation. A pathological enhancement of F-wave amplitude in abductor pollicis brevis has also been recorded in patients with median nerve entrapment (Shahani et al 1980(a)). Unfortunately, the responses from sequences of only 10 stimuli were analysed and in small numbers of control subjects as well as patients. Notably the entrapment related change in F-wave amplitude (expressed as percentage of the maximal compound muscle action potential) was found when the median minimal F-wave latency was within normal limits. This suggests that reinnervation and ongoing denervation may not have been present in these cases as it would be unusual to see denervation in a peripheral nerve entrapment syndrome not associated with an increase in the minimal F-wave latency (personal observation). The implication that F-wave amplitude can be increased by disorders of the lower motor neurone by mechanisms different from those operating to increase the amplitude in an upper motor neurone lesion is interesting, but personal observations of large numbers of F-responses in a big series of median entrapments do not confirm any obvious trend in alteration of the F-wave amplitude (no formal analysis has been made). Significantly, no further publications related to F-wave amplitude in entrapment syndromes could be found in the literature since the original work was published eight years ago.

6.5. The Prevalence of %Repeater F-wave Abnormalities in Patients with Carpal Tunnel Syndrome: An Experiment

6.5.1. Introduction

In the electrodiagnostic confirmation of carpal tunnel syndrome all methods used at the present time to study impulse conduction measure impaired nerve conduction velocity. This is done by measuring transmission latencies across nerve segments and by observing reductions in, e.g., the amplitudes of digital sensory action potentials, sensory nerve action potentials, "mixed" nerve action potentials or compound muscle action potentials which result from conduction block or abnormal temporal dispersion of nerve impulses. The results of the analysis of F-wave discharge patterns in the various types of neuropathy (see 4.3) suggest that lesions of peripheral nerves can modify the usual patterns of F-responses evoked in the healthy state. If the F-wave generating activity of a test motor neurone pool was sufficiently sensitive to the influence of an ipsisegmental peripheral nerve lesion the identification of deranged F-response patterns could provide an alternative and practicable method for the electrodiagnosis of peripheral nerve lesions.

In the cases of ulnar compression neuropathy (included in the analysis previously described) %Repeater F-wave values often remained within the control range (see Table 19) when there was evidence on conventional tests of advanced motor fibre damage. It would appear, in many of those cases, that quantifying F-response patterns would be an insensitive method of identifying a lesion in a mixed peripheral nerve. Initial observations, however, suggested that the %Repeater F-wave value was more likely to detect a lesion when the median rather than the ulnar nerve was damaged. No explanation is apparent for this observation which hints at a differential

liability of the two ipsisegmental motor neurone pools to express altered motor neurone responsiveness in the presence of a peripheral nerve lesion. If these observations were confirmed, quantification of F-response patterns using the %Repeater F-wave value would be a useful addition to the methods currrently used for the identification of median nerve entrapment.

To assess the prevalence of abnormal F-wave generating activity in the alpha motor neurones of abductor pollicis brevis in the carpal tunnel syndrome a series of patients was studied. Each patient with the carpal tunnel syndrome had confirmation of a sensory fibre lesion of the median nerve in the carpal tunnel using Kimura's "inching" technique for measuring sensory conduction in the wrist-palm segment of the median nerve (Kimura 1979). Kimura's technique was used as a yardstick against which to compare the F-wave measurements as it is a quick, technically simple, sensitive and established method of testing for median nerve fibre dysfunction. Of course, motor fibre dysfunction may not be present in all cases in which a sensory fibre abnormality is detected under the flexor retinaculum but this is not important to the aim of the experiment. Essentially the study was done on patients with carpal tunnel syndrome which had been verified electro-diagnostically using a test of sensory fibre function. In order to assess the prevalence of "advanced" motor fibre dysfunction in these cases the distal motor latency was measured.

As an age related effect on both F-wave persistence and the %Repeater F-wave value was detected in the analysis of the F-responses recorded from the abductor pollicis brevis muscles of healthy volunteers (see 2.4), the analysis in this experiment was confined to patients between the ages of 26 and 65 years. For practical purposes this meant the exclusion of elderly patients with carpal tunnel syndrome.

This experiment was done to see if quantification of F-wave discharge patterns provided a sensitive or insensitive method for detecting median nerve dysfunction resulting from compression of that nerve in the carpal tunnel.

6.5.2. Materials and methods

Subjects

Group 1. Ninety-nine healthy individuals, 46 male and 53 female, aged 26 to 63 years (mean 43, S.D. 9.8), volunteered for the study. From them, 147 median nerves/abductor pollicis brevis muscles were evaluated to obtain F-wave persistence values and %Repeater F-wave values with which the values obtained from patients with carpal tunnel syndrome could subsequently be compared. Each subject met the criteria, already described in 2.2.2, necessary for inclusion as a healthy volunteer. This group of volunteers has already been used to provide measurements used in the analysis of the effect of age on F-wave persistence and the %Repeater F-wave value.

Group 2. From Group 1, 26 subjects, 15 female and 11 male, aged 26 to 63 years (mean 39 years) were evaluated to establish "normal values" for the sensory antidromic wrist-palm latency measurement over an 8 cm segment of the median nerve across the carpal tunnel (Kimura 1979). Fifty-two median nerves were studied.

Group 3. One hundred and forty-seven hands from 71 female and 33 male patients, aged 26 to 65 years (mean 45.8, S.D. 9.3), with unilateral or bilateral carpal tunnel syndrome were evaluated. Each test hand was included in this study once a sensory antidromic wrist-palm latency value across the carpal tunnel segment $\geq$1.8 ms was confirmed. These patients were referred for electrodiagnostic tests to the EMG laboratory at Dundee Royal Infirmary, from that hospital's neurology clinic, the orthopaedic and hand clinics at Dundee Royal Infirmary, and Bridge of Earn Hospital, and rarely from rheumatology, general medical and general surgical departments, Dundee Royal Infirmary, and Ninewells Hospital, Dundee. None of these cases had evidence of an additional nervous system lesion. The electrodiagnostic evaluation which was done at the request of the referring physician included an examination to exclude generalised peripheral neuropathy. No such neuropathy was found in any of the cases included in this series (sural sensory potential and ulnar F-waves included).

Methods. The methodology for eliciting and recording F-responses was standardised and is as detailed in 2.2.2. It will, therefore, not be repeated here. The same techniques were used for control subjects and patients. Attention was paid to maintaining the volar forearm skin temperature $\geq$34°C.

One hundred F-wave sweeps were recorded from the motor point of abductor pollicis brevis in each test hand. From those photographed sweeps, F-wave persistence and %Repeater F-wave values were calculated. The methods of making these calculations are described in 2.2.2. and 2.3.2; see Figure 3, page 69 , Figure 6, page 91 and Figure 7, page 93 .

The measurement of sensory antidromic wrist-palm latency in the median nerve over the carpal tunnel segment used an 8 cm length and recordings of sensory action potentials were made using saline soaked lint

covered silver strips formed as ring electrodes over the proximal and distal interphalangeal joints of the index finger. Figure 30, page 258 illustrates, diagramatically, the "inching" technique. The distal skin crease identifies the zero point and the stimuli "inch" distally in 1 cm steps from a point 3 cm proximal to the zero point. As illustrated, focal slowing can be identified in some cases of carpal tunnel syndrome. In many, however, there is more diffuse slowing. Only the +3 and -5 latencies were measured in this study.

6.5.3. Results

The F-wave persistence and %Repeater F-wave values calculated from the F-wave sweeps in the control and carpal tunnel syndrome groups are listed in Tables 24 and 25, pages 275 to 280. To see if there were statistically significant differences in the values measured from the muscles of the two groups, the data were analysed using the Mann-Whitney test.

The F-wave persistence value for the carpal tunnel syndrome group was significantly lower than for the control group ($p<<0.0001$). F-wave persistence ranged in the control group from 25 to 100 and in the carpal tunnel syndrome group it ranged from 2 to 100. In only 6 dysfunctioning median nerves was the F-wave persistence value below the lowest value obtained in the control group.

The Repeater F-wave count recorded from an individual carpal tunnel syndrome hand ranged from 2 to 100. Characteristically, when there was a low Repeater F-wave count there was a low F-wave persistence value and if a high level of persistence was present the Repeater F-wave count was also high. The Repeater F-wave counts obtained from the damaged nerves were often in the range seen in the control nerves but there was a statistically significant difference between the values in the 2 groups ($p<0.0001$), being higher in the carpal tunnel syndrome group.

TABLE 24

F-WAVE PERSISTENCE AND %REPEATER F-WAVE VALUES CALCULATED FROM MEDIAN NERVES/ABDUCTOR POLLICIS BREVIS MUSCLES OF 147 HEALTHY VOLUNTEERS AGED 26-63 YEARS

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
1.	89	31
2.	100	0
3.	76	3
4.	100	7
5.	60	17
6.	25	24
7.	75	3
8.	90	3
9.	34	59
10.	89	13
11.	100	6
12.	78	37
13.	90	10
14.	90	10
15.	72	42
16.	88	9
17.	88	2
18.	80	8
19.	80	6
20.	80	0
21.	75	7
22.	75	11
23.	100	0
24.	85	7
25.	96	7
26.	92	5
27.	100	8
28.	100	4
29.	100	5
30.	100	3
31.	95	2
32.	90	6
33.	100	3
34.	73	15
35.	100	0
36.	87	2
37.	90	9
38.	95	8
39.	87	13
40.	92	8
41.	83	24
42.	100	6
43.	65	34
44.	81	27
45.	83	17
46.	97	13
47.	90	9
48.	90	11
49.	100	6
50.	90	7

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
51.	100	0
52.	48	4
53.	68	21
54.	75	31
55.	90	6
56.	51	41
57.	81	10
58.	90	16
59.	72	22
60.	58	60
61.	100	0
62.	98	13
63.	90	11
64.	75	28
65.	80	0
66.	53	34
67.	73	21
68.	93	6
69.	94	14
70.	90	11
71.	54	48
72.	80	33
73.	100	6
74.	67	4
75.	98	16
76.	90	27
77.	94	4
78.	86	5
79.	88	22
80.	55	4
81.	54	24
82.	98	12
83.	80	11
84.	93	6
85.	98	15
86.	100	8
87.	100	20
88.	88	6
89.	86	20
90.	90	4
91.	92	7
92.	92	18
93.	99	6
94.	99	25
95.	100	11
96.	83	19
97.	87	16
98.	84	2
99.	90	17
100.	89	19
101.	91	13
102.	81	27
103.	94	26
104.	99	4

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
105.	99	7
106.	91	10
107.	94	6
108.	78	23
109.	96	4
110.	74	9
111.	96	22
112.	91	4
113.	100	10
114.	84	14
115.	79	10
116.	82	27
117.	87	13
118.	94	23
119.	100	0
120.	75	28
121.	98	0
122.	90	12
123.	100	0
124.	95	4
125.	100	5
126.	98	6
127.	100	8
128.	87	9
129.	92	13
130.	100	15
131.	91	13
132.	100	7
133.	86	5
134.	100	4
135.	100	3
136.	91	0
137.	78	5
138.	100	7
139.	100	2
140.	85	13
141.	89	16
142.	100	8
143.	93	4
144.	100	12
145.	86	12
146.	100	0
147.	96	2

TABLE 25

F-WAVE PERSISTENCE AND %REPEATER F-WAVE VALUES CALCULATED FROM 147 MEDIAN NERVES/ABDUCTOR POLLICIS BREVIS MUSCLES OF PATIENTS WITH CARPAL TUNNEL SYNDROME AGED 26-65 YEARS

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
1.	73	80
2.	77	65
3.	72	20
4.	29	50
5.	58	49
6.	100	40
7.	80	72
8.	43	86
9.	78	64
10.	66	50
11.	92	56
12.	56	60
13.	70	50
14.	83	44
15.	30	100
16.	100	88
17.	70	85
18.	55	89
19.	2	100
20.	78	46
21.	88	55
22.	46	50
23.	75	42
24.	100	47
25.	84	100
26.	62	60
27.	45	58
28.	84	49
29.	97	41
30.	90	6
31.	30	50
32.	92	45
33.	50	80
34.	31	88
35.	56	77
36.	90	41
37.	51	60
38.	88	53
39.	89	31
40.	50	47
41.	70	52
42.	52	88
43.	82	94

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
44.	83	40
45.	49	57
46.	46	90
47.	80	41
48.	60	57
49.	71	46
50.	33	55
51.	61	67
52.	70	57
53.	52	62
54.	69	42
55.	61	46
56.	71	61
57.	39	62
58.	75	47
59.	71	62
60.	78	55
61.	97	76
62.	4	100
63.	79	41
64.	85	33
65.	71	33
66.	35	68
67.	31	89
68.	66	41
69.	66	42
70.	42	40
71.	62	62
72.	25	84
73.	94	92
74.	32	75
75.	46	67
76.	72	40
77.	70	40
78.	98	47
79.	56	50
80.	82	31
81.	50	60
82.	75	100
83.	53	83
84.	97	23
85.	94	18
86.	43	93
87.	90	40
88.	66	30
89.	52	47
90.	21	75
91.	37	65
92.	28	64
93.	69	50
94.	68	50

Nerve No.	F-wave Persistence Value	%Repeater F-wave Value
95.	65	50
96.	100	100
97.	97	33
98.	43	86
99.	80	100
100.	50	47
101.	60	54
102.	72	68
103.	85	40
104.	85	56
105.	86	60
106.	51	72
107.	58	52
108.	33	85
109.	70	52
110.	2	100
111.	75	100
112.	50	55
113.	43	58
114.	80	73
115.	85	82
116.	47	85
117.	37	51
118.	89	26
119.	98	8
120.	66	79
121.	85	47
122.	60	50
123.	53	62
124.	85	5
125.	95	22
126.	65	13
127.	60	10
128.	40	65
129.	92	16
130.	44	75
131.	32	100
132.	54	63
133.	39	25
134.	57	77
135.	100	100
136.	32	74
137.	65	72
138.	50	48
139.	78	12
140.	9	100
141.	58	74
142.	55	87
143.	60	90
144.	42	50
145.	51	28
146.	64	47
147.	19	100

When the %Repeater F-wave values of the two groups were compared, using the Mann-Whitney test, the values calculated from the F-wave sweeps recorded from the carpal tunnel syndrome group were significantly greater ($p<<0.0001$). These results are illustrated in bar histogram form in Figure 32.

The highest %Repeater F-wave value in the control group was 60%. It can be seen from the bar histogram that the %Repeater F-wave values in the control group were skewed.

A number of different F-wave patterns recorded from the carpal tunnel syndrome group are shown in Figure 33. Although Repeater F-waves occurring with pathological persistence levels usually appeared at delayed latencies, e.g. Figure 33, in some cases they were conducted in the normal latency range. The analysis did not take into account Repeater F-waves appearing "in series", a phenomenon described in Chapter 4.3. Figure 34 shows how a highly persistent Repeater F-wave can follow a normal pattern of initial F-responses in an entrapped nerve. This pattern was not observed in the control group in which more than one distinct F-wave component in the single F-wave sweep was not observed in more than 6 nerves, and in these the responses were not Repeater F-waves and were very infrequent.

Cumulative frequency curves were constructed from the %Repeater F-wave values obtained from the control and carpal tunnel syndrome groups. These are contained in Figure 35 (data in Table 26, page 286). The 95 percentile %Repeater F-wave value in the control reference range was 34%. 88% of %Repeater F-wave values in the carpal tunnel syndrome group were above the 95 percentile value for the control range.

The range of latencies for the sensory antidromic wrist-palm latency values in the control group was 1.1 - 1.7 ms. The mean latency was 1.49 msec (S.D. 0.157).

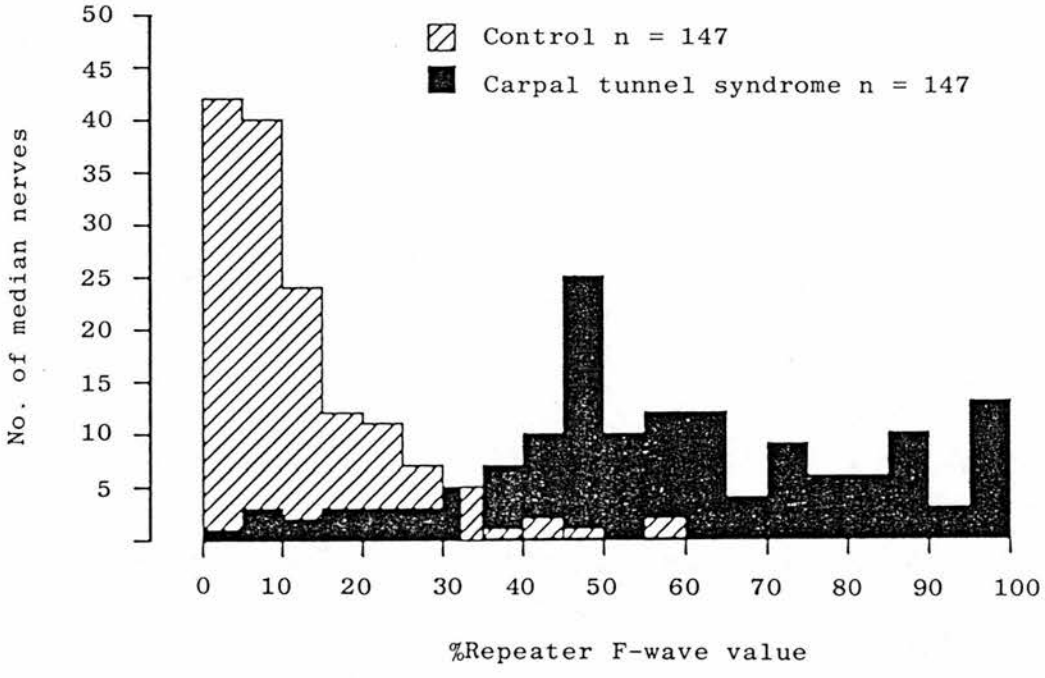
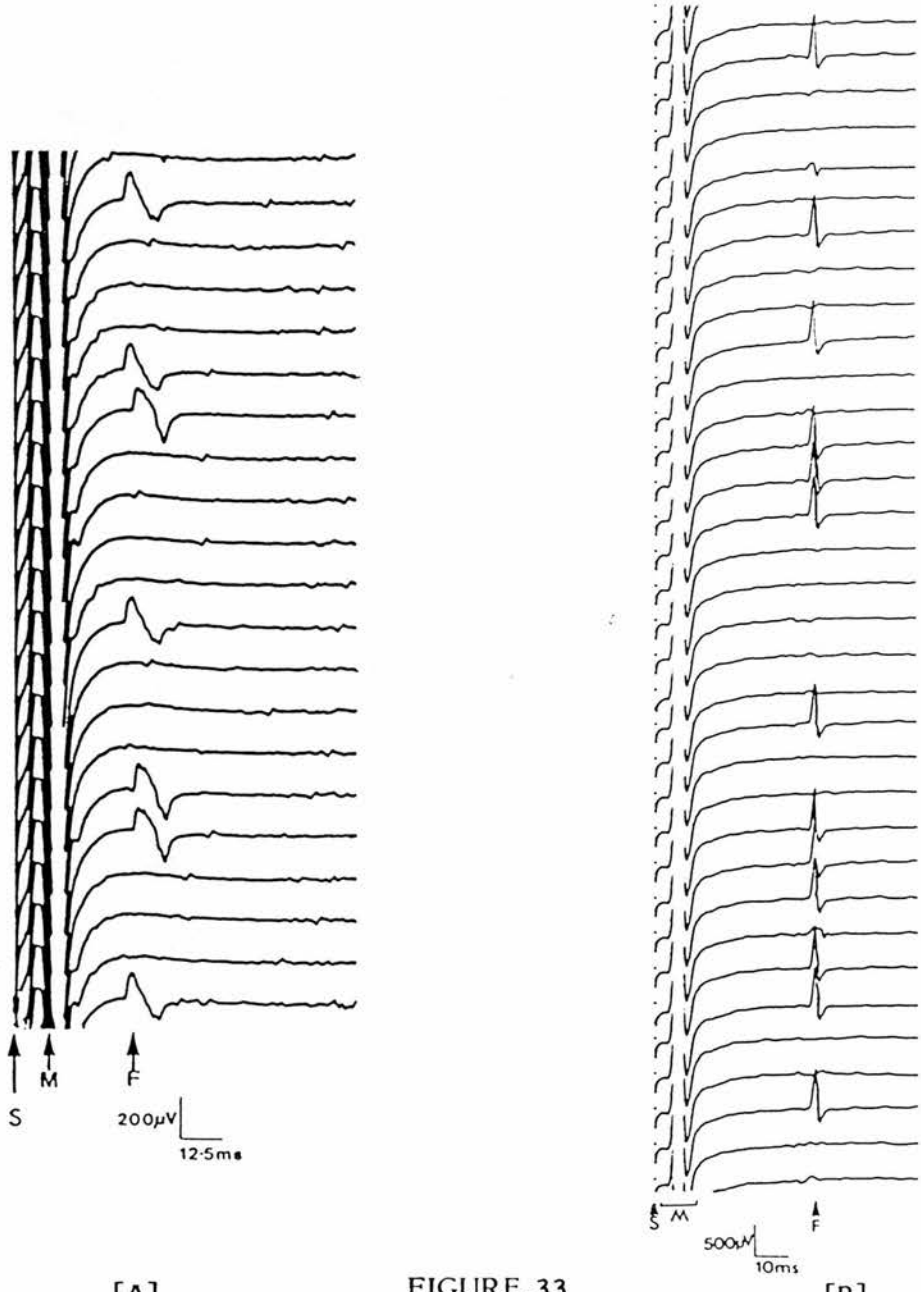


FIGURE 32

%Repeater F-wave values derived from the abductor pollicis brevis muscles/median nerves of age-matched healthy volunteers and patients with symptomatic carpal tunnel syndrome.



[A] [B]

FIGURE 33

PATHOLOGICAL F-WAVE PATTERNS IN CARPAL TUNNEL SYNDROME

A and B recorded from abductor pollicis brevis of 2 patients with a median nerve lesion in the carpal tunnel.

A: 100% Repeater F-wave value comprised of 2 individual types of Repeater F-wave.

B: Pathologically high %Repeater F-wave value. One of the Repeater waves appears persistently. F-responses are pathologically delayed.

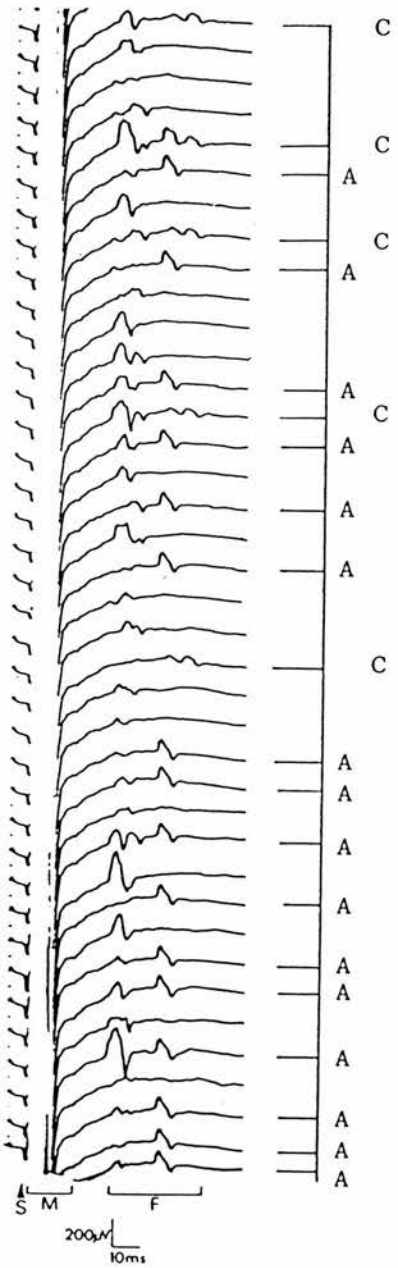


FIGURE 34

REPEATER F-WAVES "IN SERIES": CARPAL TUNNEL SYNDROME

F-wave sweeps recorded from abductor pollicis brevis. Earliest conducted F-responses give a normal %Repeater F-wave value, ignoring the F-waves which follow the earliest one on each sweep. These are followed by a persistent Repeater F-wave (A) and a less persistent and slower conducted Repeater F-wave (C).

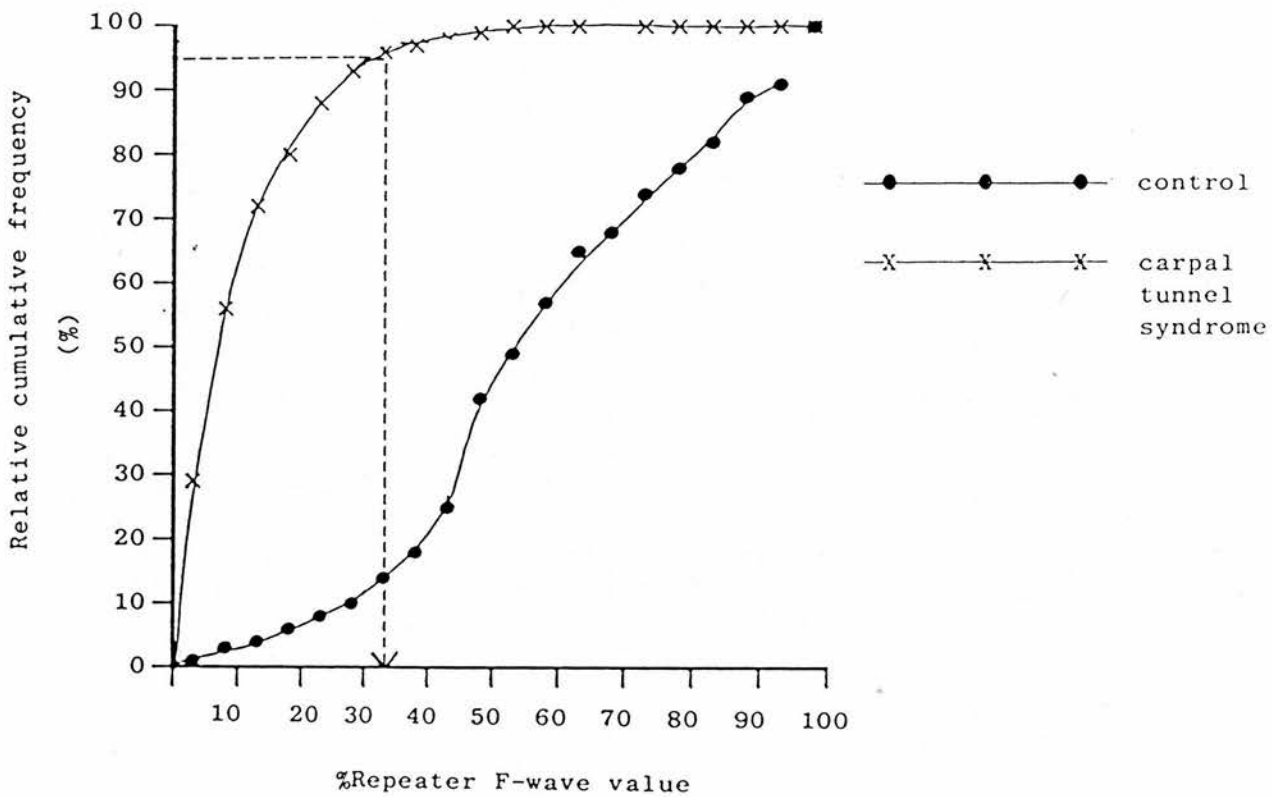


FIGURE 35

Relative cumulative frequency curves of the %Repeater F-wave values in Tables 24 and 25, derived from the abductor pollicis brevis muscles/median nerves (n = 147) of patients with symptomatic carpal tunnel syndrome and a group of age-matched healthy volunteers (n = 147).

The 95 percentile value for the reference range is indicated by dotted line and arrow (34%).

TABLE 26

RELATIVE CUMULATIVE FREQUENCY VALUES FOR %REPEATER F-WAVE VALUES IN 147 HEALTHY AND 147 DAMAGED MEDIAN NERVES

	CONTROLS (n = 147)		CARPAL TUNNEL SYNDROME (n = 147)	
%Repeater F-wave value	No. of nerves	Relative cumulative frequency (%)	No. of nerves	Relative cumulative frequency (%)
0-5	42	28.6	1	0.7
6-10	40	55.8	3	2.7
11-15	24	72.1	2	4
16-20	12	80.3	3	6
21-25	11	87.8	3	8.2
26-30	7	92.5	3	10.2
31-35	5	95.9	5	13.6
36-40	1	96.5	7	18.4
41-45	2	98.0	10	25.2
46-50	1	98.6	25	42.2
51-55	0	"	10	49
56-60	2	100	12	57.1
61-65	0	"	12	65.3
66-70	0	"	4	68
71-75	0	"	9	74.1
76-80	0	"	6	78.2
81-85	0	"	6	82.3
86-90	0	"	10	89.1
91-95	0	"	3	91.2
96-100	0	"	13	100

Distal motor latency was <4.5 msec in 61% of carpal tunnel syndrome cases and >4.8 msec in 32% of cases.

6.5.4. Comment and conclusions

Kimura's test of sensory conduction through the carpal tunnel is sensitive and quick to perform. For these reasons it was used to identify nerve fibre dysfunction in hands with symptoms of carpal tunnel syndrome. Although it is inappropriate to make a direct comparison between the F-wave technique and Kimura's sensory fibre technique for detecting median nerve lesions the comparison of the two can at least provide a rough gauge as to the sensitivity of the %Repeater F-wave value in identifying median nerve lesions in symptomatic hands. Of course, many of the nerves assessed did not have a prolonged distal motor latency and in some there may have been no motor fibre lesion. However, accepting the obvious limitations of such a comparison, it would appear from these results that the %Repeater F-wave measurement can detect more lesions than the distal motor latency measurement and it detected a lesion in the majority of nerves in which the sensory antidromic wrist-palm latency measurement was abnormal (using the 95 percentile value of the control reference range). Almost 90% of the %Repeater F-wave values calculated from the F-responses issued through the damaged nerves exceeded the 95 percentile value in the control reference range. Direct comparisons between the senosry fibre test of Kimura and F-wave quantification are inappropriate as they test different things. (The possibility that sensory lesions in a peripheral nerve can modify patterns of F-wave production is considered in 4.3.4).

It is clear that significant numbers of patients with atypical presentations of carpal tunnel syndrome cannot be diagnosed clinically with accuracy (see 6.7) and some are likely to escape identification by the nerve conduction study techniques currently in use (see 6.1 and 6.2). As the %Repeater F-wave value quantifies an additional and distinct aspect of neuronal dysfunction (i.e. the responsiveness of the motor neurone pool of abductor pollicis brevis to backfired motor impulses) it is tempting to hope that additional cases might be detected through its use (see 5.3 and 5.4).

One patient was encountered outside this study who had symptoms compatible with carpal tunnel syndrome whose sensory antidromic wrist-palm latency value was normal while the abductor pollicis brevis %Repeater F-wave value was 80% and the distal motor latency was 5.2 ms. This shows that sensory fibres can be spared when motor fibres are compromised under the transverse carpal ligament and that the %Repeater F-wave value can indicate an entrapment when the sensory antidromic wrist-palm latency measurement remains within normal limits (see 5.4). That case also illustrates the importance of measuring distal motor latency even though the distal motor latency is a "false-negative" in a high percentage of cases. The author has also encountered some cases in which the %Repeater F-wave value was found to be high at the time of initial presentation, while the sensory antidromic wrist-palm latency measurement was normal, but on follow-up the sensory wrist-palm latency measurement was found to be pathological after the passage of some time.

The measurements of F-wave persistence and the Repeater F-wave counts, taken as isolated measurements, were seen (as in the peripheral neuropathies previously described in Chapter 4) to be insensitive in detecting nerve lesions. The %Repeater F-wave values reflected the group tendency to a reduction in F-wave persistence and an increased liability to

generate Repeater F-waves and, as a single measurement, is a readily computed index of altered F-wave production.

Some speculative comments on the mechanisms which might underly these observations are to be found in 4.3 and 6.6.

6.6. F-wave Discharge Patterns Evoked by Stimuli Proximal and Distal to a Segmental Peripheral Nerve Lesion: An Experiment

6.6.1. Introduction

How F-wave production is modified when a mixed peripheral nerve is compressed is uncertain. Some possible contributory mechanisms are discussed in Chapter 4. One factor which was considered concerns the effect of an alteration in the profile of the antidromic motor volley as it invades the motor neurones under test. If this was an important mechanism, it is possible, that by moving the nerve stimulus from a position proximal to a segmental lesion to a site distal to the lesion, the profile of the antidromic volley would be rendered more abnormal, resulting in a more pathological pattern of responsiveness in the test motor neurone pool. Resulting from this change in stimulus site, the fastest conducting alpha axons might fail to transmit impulses to the cord from the more distal stimulus site while they continue to conduct impulses antidromically from the proximal stimulus site. Additionally, the nerve volley could be more temporally dispersed than normal if slowing of conduction was present in a proportion of the axons. (Of course, in carpal tunnel entrapments of the median nerve, demyelination can extend proximally and affect the nerve at the point where the electrical stimulus is conventionally applied, just proximal to the proximal edge of the transverse carpal ligament) (Gilliatt and Harrison 1984). Theoretically, the loss of Renshaw inhibition mediated via the largest motor neurones might have significant effects on the responsiveness of slower conducting motor neurones to antidromic volleys conducted by their intact axons. Other effects could be predicted in the presence of nerve block, e.g. diminished F-wave persistence and a reduction in the fraction of the test motor neurone pool capable to participating in the F-response. However, the initial concept

which was described above led to the experiment which follows. It tests the hypothesis that stimuli delivered proximal and distal to a segmental peripheral nerve lesion might result in normal and pathological F-response patterns, respectively.

The hypothesis has been tested by quantifying F-wave discharge patterns evoked by stimuli proximal and distal to the transverse carpal ligament in patients with symptomatic carpal tunnel syndrome, verified by conventional nerve conduction studies.

The material in the experiment does not provide an ideal experimental model. The patients were selected as they had typical presentations of carpal tunnel syndrome and there were no features present (clinical or electrodiagnostic) suggestive that a second lesion was present. It can be anticipated that demyelination may have extended proximally, in some cases, to the site of the proximal stimulus, while in others it would not. There is also a variable amount of axonal degeneration present in the test population (this has not been quantified). No quantification was done of the extent of any motor fibre lesion, which might have been present, in the carpal tunnel segment. It may be that in some instances there was no motor fibre lesion. The material used in the experiment is therefore not standardised. However, the essential aim of the experiment was to determine if, in some cases of carpal tunnel syndrome (even a small number), a normal F-wave discharge pattern might be recorded with a proximal stimulus while a distal stimulus evoked a pathological pattern of F-responses. The second aim was to determine if differences in F-response patterns evoked by stimuli proximal and distal to the carpal tunnel occurred in the healthy state.

It has already been shown that a proximal stimulus can identify alterations in the F-discharge behaviour of motor neurones of abductor pollicis brevis, in the presence of a lesion of the median nerve in the carpal

tunnel (see 6.5).

If a distal stimulus could result in a pathological pattern of F-responses, while a proximal one did not, the technique could be used, firstly, to identify peripheral mixed nerve lesions and secondly, to accurately site the lesion in the nerve segment between the two stimuli.

6.6.2 Materials and methods

Subjects

Twenty-nine median and 29 ulnar nerves from 17 female and 12 male patients with sympatomatic carpal tunnel syndrome were studied. These patients ages ranged from 30 to 62 years (mean 43).

All had electrodiagnostic confirmation of median nerve dysfunction localised to the carpal tunnel segment of the median nerve using the conventional nerve conduction and electromyographic techniques employed in day to day practice. (This included ulnar and median "mixed" nerve studies over the palm-wrist and forearm segments, ulnar and median nerve F-wave latencies evoked from the wrist and recorded from abductor digiti minimi and abductor pollicis brevis muscles, median sensory antidromic wrist-palm latency measurement, distal motor latency, motor nerve conduction velocity over the forearm segment of the median nerve and electromyography of intrinsic hand and, if necessary, forearm muscles).

A neurological history and examination did not suggest the presence of any additional neurological disorder beyond carpal tunnel syndrome. None had any illnesses which predisposed to peripheral neuropathy and none were exposed to neurotoxic drugs. The subjects studied were therefore uncomplicated cases of carpal tunnel syndrome in which a lesion (not necessary of motor fibres) have been identified by one or more conventional nerve

conduction study abnormalities. The patients were consecutive cases, who attended this EMG laboratory, meeting the inclusion criteria for the study.

Forty-one median nerves and 41 ulnar nerves from 24 healthy volunteers, 13 females, 11 male, aged 19 to 68 years (mean 36) were studied. (Two subjects were aged less than 30 years and one was aged over 65 years). None had any identifiable predisposition to peripheral neuropathy. Each had a neurological examination of the test upper and lower limbs: no abnormalities were found in any. Distal motor latency and sensory antidromic wrist-palm latency (Kimura 1979) were measured in each volunteer and all fell within the laboratory's control range (see 6.5).

Methods

The equipment used in this experiment differs slightly from the previous experiments. All F-wave recordings were obtained, in both the control and carpal tunnel subjects, using an identical silver/silver chloride disc electrode (E.E.G. type, Medelec type E/RE-K5306, diameter 0.99 mm) taped to the motor point of abductor pollicis brevis. The reference electrode (the same type of disc electrode) was applied over the muscle's tendon and the earth was placed at a site which optimised the quality of the recording, usually at the base of the index finger on its volar aspect. The temperature of the volar aspect of the test forearm was maintained at or above 34°C during the test.

Electrical stimuli were delivered at three sites in each test limb; two sites on the median nerve and one site on the ulnar nerve. The F-responses evoked from the three stimulation sites in each subject were all recorded from the same electrode over the motor point of abductor pollicis brevis.

The following protocol was followed in each test hand: Firstly, with the stimulus over the median nerve, just proximal to the distal skin crease of the wrist, a maximised M wave was recorded from abductor pollicis brevis. The cathode was then placed in a proximal position (i.e. cathodal and anodal placements were reversed and the amplitude of the M-wave was rechecked). The technique for recording F-wave sweeps will not be described in full here as it is already contained in 2.2. i.e. each patient was supine and relaxed and told to request a break if they desired one). One hundred stimuli (20% supramaximal for the maximal M-wave) were applied at this site and the F sweeps were photographed from the oscilloscope for subsequent analysis. Next, the stimulating electrode was moved to the palm of the hand and the position found where the thenar branch of the median nerve could be stimulated to produce an M-wave at least as large as that evoked at the initial stimulus site, proximal to the wrist. (The size of the M response evoked from the palm of the hand was often larger than the M response evoked more proximally in the carpal tunnel group). One hundred (20% supramaximal) stimuli were then applied at this site with the cathode placed proximal to the anode. The resultant F-wave sweeps (100) were recorded for analysis. Finally, 50 stimuli (20% supramaximal for the M-wave) were applied to the ulnar nerve at the wrist just proximal to the distal skin crease and the F-responses obtained at the motor point of abductor pollicis brevis were again recorded using the same electrode. Figure 36 illustrates how F-waves can be recorded from ulnar-innervated thenar muscle through the bulk of abductor pollicis brevis. Inadvertent stimulation of the branch of the ulnar nerve to adductor pollicis in the palm could, theoretically, result in recording F-waves from the surface electrode over the motor point of abductor pollicis brevis.

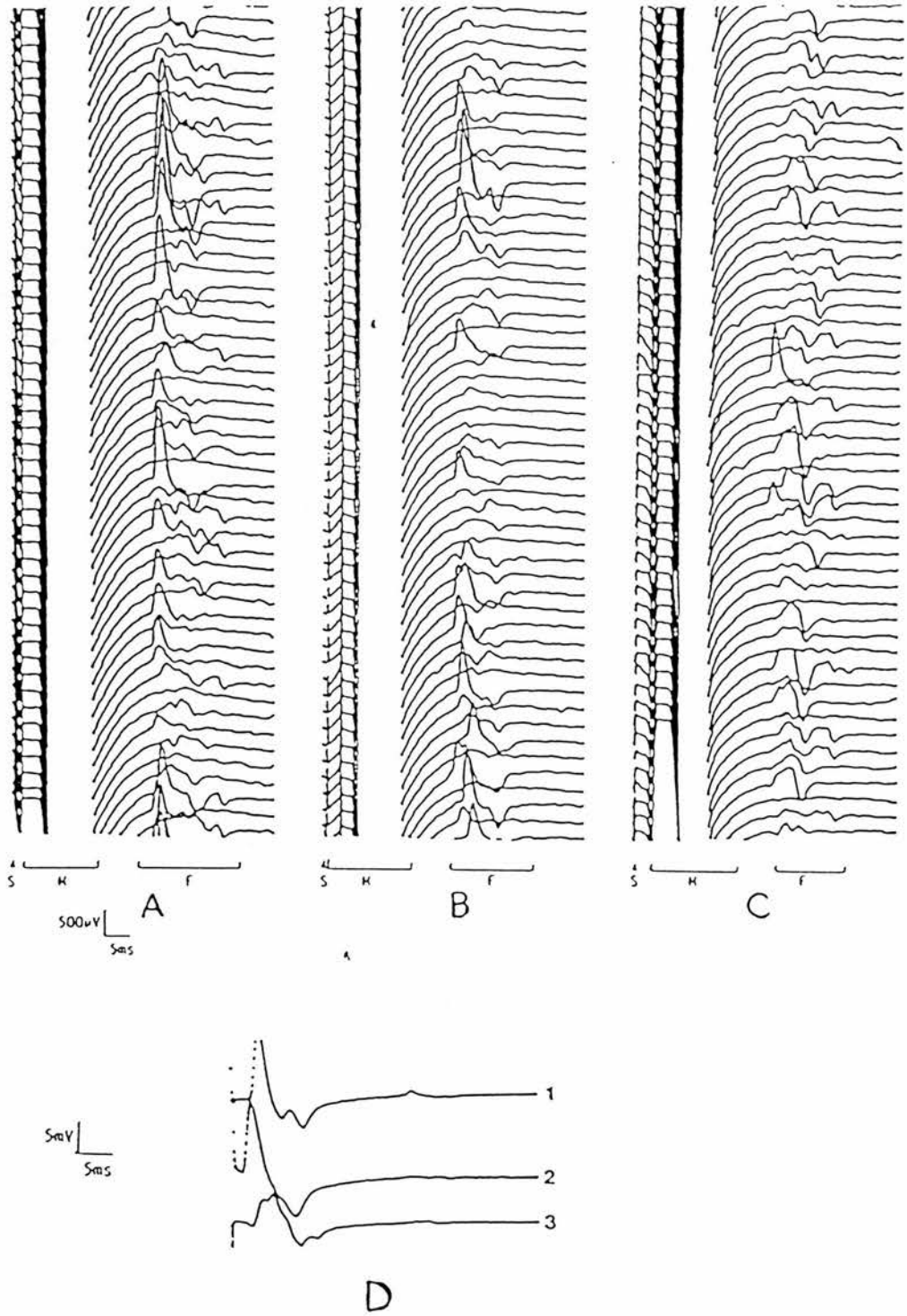


FIGURE 36

M and F-waves recorded from the motor point of abductor pollicis brevis stimulating the median and ulnar nerves of a healthy volunteer.

D1/B M and F-waves stimulating the median nerve at the wrist;
D3/C M and F-waves stimulating the ulnar nerve at the wrist;
D2/A M and F-waves stimulating the thenar branch of the median nerve distal to the carpal tunnel.

The F-response sweeps were recorded on photographic paper using a Medelec MS8 electromyograph as detailed in the description of methodology in 2.2. The methods used to calculate F-wave persistence and %Repeater F-wave values are contained in 2.2.2 and 2.3.2 on pages 68 and 92.

6.6.3. Results and Statistical Analysis

F-wave persistence and the %Repeater F-wave values obtained from abductor pollicis brevis with the stimulus on the median nerve, proximal and distal to the tranverse carpal ligament, are listed in Tables 27 and 28 on pages 297 and 298.

In the control group individual nerves showed a maximal rise in %Repeater F-wave value across the carpal tunnel of 15 (no. 33) and a maximal drop of -23 (no. 16). (Parenthetically, the %Repeater F-wave values obtained from the palm and wrist stimuli all fell within the 95 percentile value of the control range (see 6.5.3) elicited by a stimulus just proximal to the transverse carpal ligament. It should, however, be remembered that a different type of surface recording electrode (similar diameter) was used in this experiment from that used to establish a control range in 6.5.3. However, similar values were obtained in this experiment from healthy volunteers as were obtained previously. The largest drop in F-wave persistence in an individual control nerve was -28 (no. 5). F-wave persistence values obtained by stimulating the thenar nerve distal to the carpal tunnel were ≥ 44. To see if there was a significant difference in the mean F-wave persistence values elicited by the proximal and distal stimuli a paired t-test was applied. As a first step, a scatter diagram of the measurements obtained with stimuli at wrist and palm sites, was plotted to determine the trend was near 45°. The same analysis was then applied to the %Repeater F-wave

TABLE 27

%REPEATER F-WAVE VALUES AND F-PERSISTENCE VALUES FROM ABDUCTOR POLLICIS BREVIS, WRIST AND PALM STIMULI: AN EXPERIMENT

CONTROL
(n = 41)

Nerve No.	%Repeater F-wave value		F-wave persistence		Absolute change in %Repeater F-wave value across carpal tunnel
	Wrist stimulus	Palm stimulus	Wrist stimulus	Palm stimulus	
1	22	10	88	90	-12
2	6	0	88	91	- 6
3	15	9	52	51	- 6
4	3	14	54	44	+11
5	10	11	74	46	+ 1
6	0	6	67	70	+ 6
7	18	23	70	59	+ 5
8	26	7	66	70	-19
9	6	4	87	83	- 2
10	0	0	83	77	0
11	6	0	98	94	- 6
12	8	6	82	90	- 2
13	3	2	90	98	- 1
14	0	3	100	94	+ 3
15	10	9	72	77	- 1
16	30	7	52	55	-23
17	2	0	91	93	- 2
18	0	7	81	88	+ 7
19	0	0	91	89	0
20	0	6	100	88	+ 6
21	5	0	91	99	- 5
22	0	0	97	98	0
23	3	6	93	85	+ 3
24	15	12	88	82	- 3
25	3	11	91	92	+ 8
26	0	3	88	94	+ 3
27	11	9	71	80	- 2
28	18	22	85	72	+ 4
29	6	3	95	78	- 3
30	12	19	85	75	+ 7
31	17	18	95	82	+ 1
32	9	2	77	87	- 7
33	2	17	97	84	+15
34	3	7	77	93	+ 4
35	4	9	90	98	+ 5
36	8	3	95	93	- 5
37	2	6	97	97	+ 4
38	12	19	95	88	+ 7
39	21	16	99	96	- 5
40	13	12	85	70	- 1
41	26	21	94	91	- 5
Mean	8.7	8.3	84.6	82.4	
SD	8.1	6.7	12.8	14.4	

TABLE 28

%REPEATER F-WAVE VALUES AND F-WAVE PERSISTENCE VALUES FROM ABDUCTOR POLLICIS BREVIS USING WRIST AND PALM STIMULI

MEDIAN NERVES: CARPAL TUNNEL SYNDROME
(n = 29)

Nerve No.	%Repeater F-wave Value		Absolute change in %Repeater F-wave value across carpal tunnel	F-wave Persistence	
	Wrist stimulus	Palm stimulus		Wrist stimulus	Palm stimulus
1	42	100	+58	83	100
2	80	100	+20	55	24
3	70	37	-33	30	38
4	45	36	- 9	77	27
5	47	84	+37	74	19
6	33	83	+50	73	30
7	60	56	- 4	80	36
8	82	100	+18	34	12
9	41	93	+52	66	28
10	32	72	+40	25	36
11	25	63	+38	92	70
12	78	100	+22	54	19
13	33	100	+67	85	72
14	32	38	+ 6	100	69
15	73	55	-18	26	60
16	52	90	+38	65	78
17	33	33	0	79	82
18	39	41	+ 2	82	56
19	71	100	+29	51	39
20	49	83	+34	57	24
21	18	26	+ 8	84	82
22	27	51	+24	83	72
23	6	11	+ 5	92	100
24	21	58	+37	65	29
25	24	69	+45	51	32
26	8	9	+ 1	78	88
27	13	15	+ 2	95	98
28	19	21	+ 2	89	85
29	28	74	+46	60	31
Mean	40.7	62		68.4	53
S.D.	21.7	29.9		20.7	27.7

values. This showed there was no statistically significant difference in either measurement when they were made at the two sites ($p=0.73$, $p=0.12$ respectively).

Group of damaged nerves. To see if there were significant differences in F-wave persistence and the %Repeater F-wave values calculated from the F-wave sweeps obtained with the stimuli proximal and distal to a damaged nerve segment, paired t-tests were applied to the data obtained from the carpal tunnel syndrome group. The %Repeater F-wave values were increased significantly ($p<<0.0001$) and F-wave persistence decreased significantly ($p=0.001$) when the stimuli were delivered distal rather than proximal to the carpal tunnel. Figure 37 illustrates how, in an individual muscle, the %Repeater F-wave value can become pathological when the stimulus is moved distal to the segmental lesion.

The lowest persistence value recorded with the palmar stimulus in the group of damaged nerves was 12 but, not uncommonly, F-wave persistence was retained at a value at the high end of the normal range (i.e. the range seen in the 41 control nerves). In some individual damaged nerves the F-wave persistence value did not decrease but increased when the stimulus was moved to the distal site, e.g. no. 15. In one damaged nerve, with a borderline wrist evoked %Repeater F-wave value (no. 10) but a pathological palm evoked %Repeater F-wave value, F-wave persistence also rose when the stimulus moved distally to the palm. In another damaged nerve, (no. 16), the pathological %Repeater F-wave value, which was more abnormal when elicited by the distal stimulus, was associated with an increase in F-wave persistence rather than a decrease.

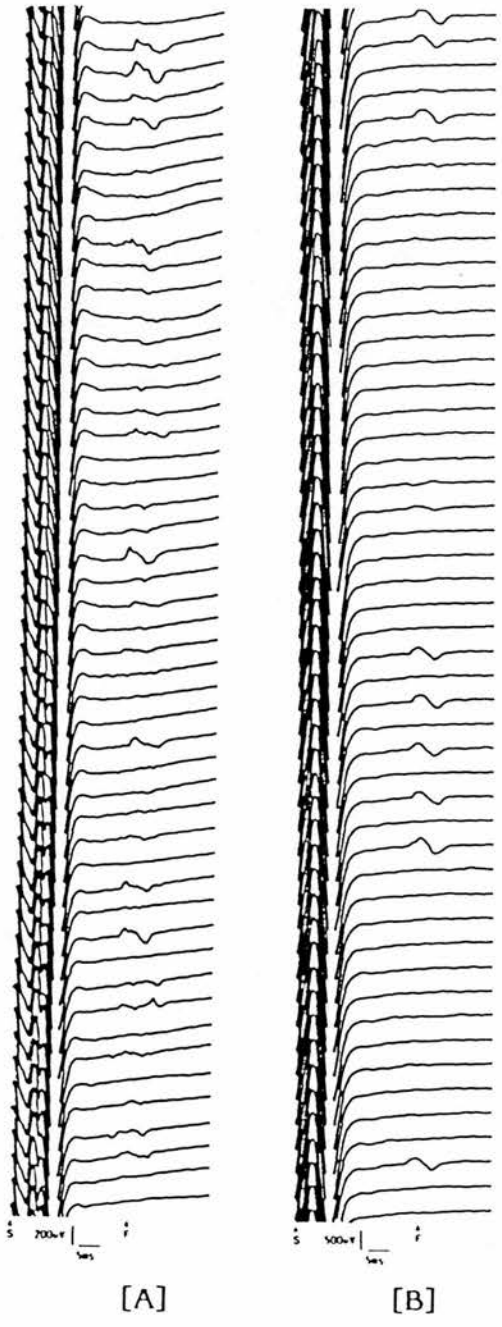
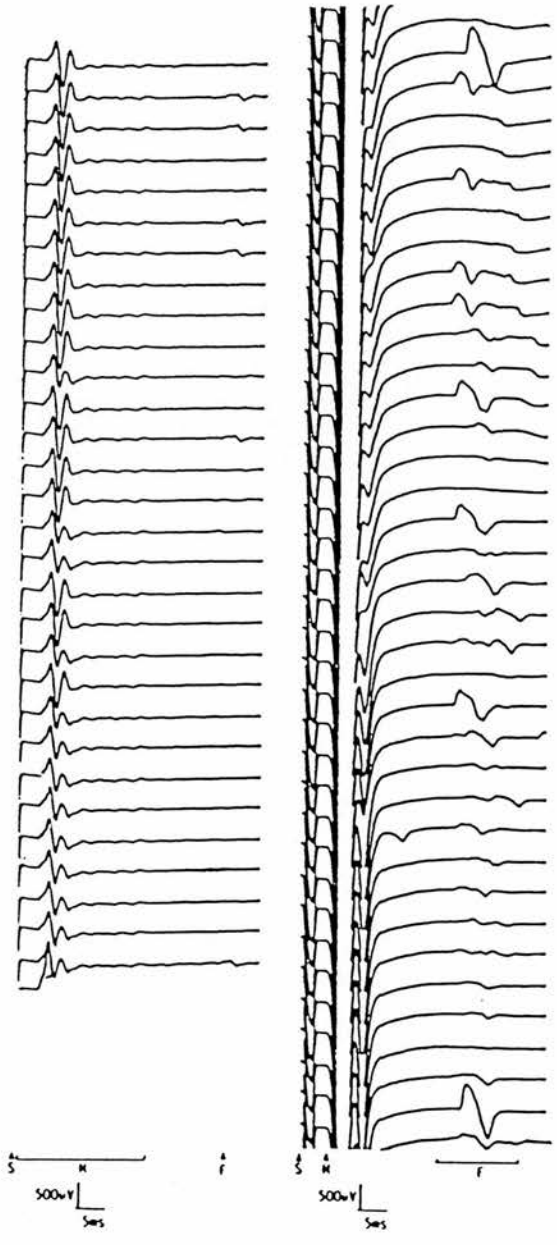


FIGURE 37

DIFFERENCES IN A MOTOR NEURONE POOL'S F-WAVE GENERATING ACTIVITY WHEN THE ANTIDROMIC VOLLEY IS SET UP PROXIMAL AND DISTAL TO A SEGMENTAL MIXED NERVE LESION

F-responses from a patient with carpal tunnel syndrome. F-waves recorded from the same disc electrode over the motor point of abductor pollicis brevis stimulating the median nerve [A] proximal to, and[B], distal to, the carpal tunnel. The %Repeater F-wave value is within the control range when evoked by the proximal stimulus but is beyond the upper value seen in the control range when the stimulus is moved into the palm.

The 50 F-response sweeps which were recorded when the stimulus was delivered to the ulnar nerve at the wrist were scrutinised to see if F-wave persistence, %Repeater F-wave values and individual F-wave forms were similar or dissimilar to those recorded when the stimulus was located in the palm. In different individuals, ulnar-evoked F-responses with low and high persistence levels were detected. Figure 36 showed ulnar nerve activated F-waves which were highly persistent. %Repeater F-wave values were invariably low (<25%) when the stimulus was over the ulnar nerve at the wrist. When, in the carpal tunnel syndrome hands, high %Repeater F-wave values were obtained with the palm stimulus, those responses could be differentiated from the ulnar evoked F-responses by amplitude, configuration, persistence and %Repeater F-wave values. Figure 38 provides an example of how F-wave latency, configuration, persistence and the calculated %Repeater F-wave values can all be different when the ulnar nerve is stimulated at the wrist and the median nerve stimulated in the palm in carpal tunnel syndrome. [A] shows the small amplitude, M and F-responses recorded from the motor point of abductor pollicis brevis in a patient with carpal tunnel syndrome who, two years earlier, had a transposition of the ipsilateral ulnar nerve as treatment for a tardy ulnar palsy. Long-standing wasting was present in the ulnar nerve territory and an individual Repeater F-wave appears impersistently (at 41 ms). This response is recorded from adductor pollicis through the bulk of abductor pollicis brevis. Were the stimulus delivered to the ulnar branch to adductor pollicis in the palm its latency would be even greater. The F-waves recorded from the same site, stimulating the thenar nerve in the palm, consist of multiple Repeater F-waves, which are more persistent and can, at 31-33 ms, be clearly distinguished from those in adductor pollicis. The %Repeater F-wave value calculated from the F-waves evoked by 100 palmar stimuli was 53%.



[A] FIGURE 38 [B]

F-WAVES TRANSMITTED BY ULNAR AND MEDIAN NERVES RECORDED FROM THE THENAR EMINENCE

The ulnar nerve had been transposed 2 years earlier for tardy ulnar palsy. Currently, patient has symptoms of ipsilateral carpal tunnel syndrome. Longstanding muscle wasting was present in ulnar nerve territory.

A: Stimulus to the ulnar nerve at the wrist: The impersistent Repeater F-responses are pathologically delayed (Ca. 41 ms).

B: Stimulus to the median nerve in the palm: F-waves (31-33 ms), different in latency and form, are readily distinguished from F-waves evoked by the ulnar nerve stimulus. Note palmar activation of F-responses in adductor pollicis would yield responses >41 ms latency.

The median nerve's F-responses yield a pathological %Repeater F-wave value (from 100 F-sweeps).

Differentiation between the F-discharges evoked by ulnar nerve stimulation and those evoked by the palmar stimulus was most readily made when palmar (median nerve) stimuli resulted in the recording of impersistent F-waves with a high %Repeater F-wave value and ulnar nerve stimuli generated persistent F-waves with low %Repeater F-wave values. This pattern is illustrated in Figure 39.

When a pathological palm-evoked %Repeater F-wave value was obtained in any of the cases in this study, the F-responses were readily distinguishable in terms of configuration, persistence and %Repeater F-wave value from the ulnar evoked F-responses recorded from the same electrode.

6.6.4. Comments and conclusions

Significant reductions in F-wave persistence and increases in %Repeater F-wave values resulted when the stimulus was moved from a position proximal to the carpal tunnel to one distal to it in the carpal tunnel group. In that group of damaged median nerves the majority of test nerves showed an increase in %Repeater F-wave values when the stimulus was moved from "above" to "below" the lesion. There were, notably, individual nerves which displayed increased F-wave persistence as well as an increased %Repeater F-wave value when the stimulus was moved distally. This is in keeping with the observations on peripheral neuropathies (see 4.3) in which facilitation of grouped recurrent discharges through some motor neurones was identified.

A surface electrode over the motor point of abductor pollicis brevis could record F-responses from distant ulnar innervated muscle if the palm stimulus were to inadvertently activate the ulnar nerve branch supplying adductor pollicis. This does not appear to be a major drawback to the technique, although the possibility of this happening must be borne in mind.

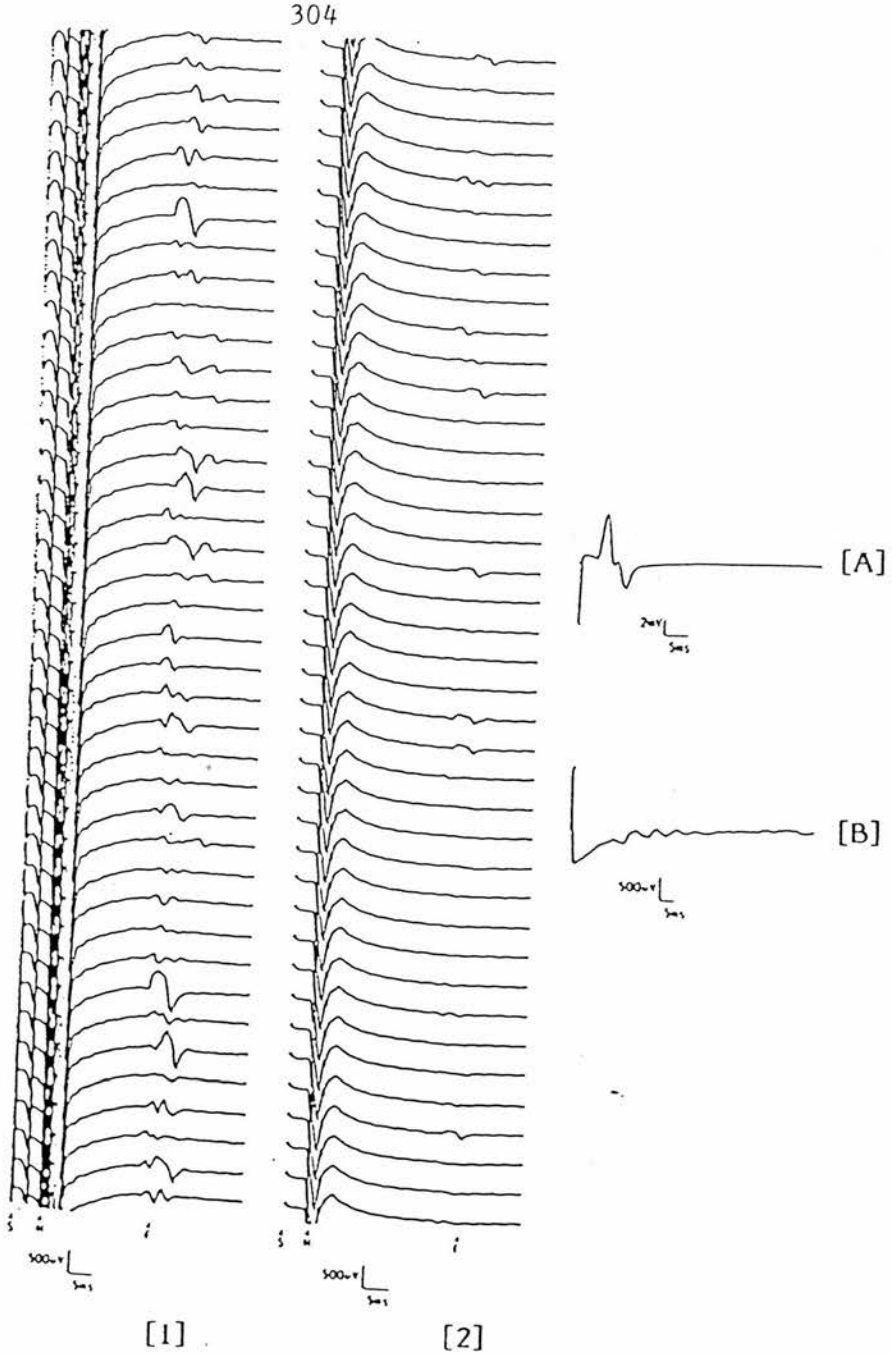


FIGURE 39

THE DIFFERENTIATION OF ULNAR AND MEDIAN NERVE EVOKED F-WAVES RECORDED FROM ABDUCTOR POLLICIS BREVIS

F-responses recorded from the motor point of abductor pollicis brevis in a case of carpal tunnel syndrome.

[1][A]: shows the F- and M waves evoked by ulnar nerve stimuli at the wrist. High persistence F-responses are seen yielding a low %Repeater F-wave value.

[2][B]: B shows the small prolonged M wave evoked by a wrist stimulus to the median nerve. [2] shows the pathological F-discharge pattern evoked from the thenar nerve distal to the carpal tunnel with a very high %Repeater F-wave value and impersistent F-waves. The M wave evoked by the palm stimulus is larger than the M evoked more proximally due to conduction block.

In the patients tested in this study there was usually (and always in those patients with a pathological %Repeater F-wave value evoked by a palm stimulus) an obvious difference in the patterns of recurrent responses evoked by the palm stimulus (over the thenar branch of the median nerve) and those evoked by the ulnar stimulus at the wrist. This difference was most obvious when the palm stimulus (presumably activating thenar nerve) evoked F-responses with a low level of persistence and with a high %Repeater F-wave value, while the F-response pattern evoked by the stimuli to the ulnar nerve had a high level of persistence and a low %Repeater F-wave value.

The palm stimulus is less uncomfortable than the wrist stimulus and was well tolerated.

Case 13 illustrates how a borderline %Repeater F value evoked by a stimulus proximal to the site of maximal nerve dysfunction can be raised to a level above that in the control range by stimulating distal to the carpal tunnel. Case 29 shows that the distal stimulus may detect a lesion while the proximal stimulus may fail to. In that hand, antidromic impulses generated patterns of F-responses such as were seen in health when set up proximal to the lesion, but resulted in a pathological pattern of F-discharges when they crossed the damaged nerve segment. The cases in which both the proximal and distal stimuli gave normal %Repeater F-wave values, e.g. nos. 23 and 26, do not necessarily represent false-negative tests as there may have been no motor fibre dysfunction in those nerves (in both those cases distal motor latency and F-latency values were within normal limits and no electromyographic signs of denervation were detected, only a sensory fibre lesion was detected). Comment has already been made in the introduction to this study that no quantification of the amount of motor fibre dysfunction in the carpal tunnel segment of the test median nerves was made. It was assumed

that an adequate number of motor lesions would be present in the test nerves to test the hypothesis.

The technique, therefore, provides an alternative to latency testing for both the identification and localisation of a peripheral nerve lesion. The presence of a pathologically high %Repeater F-wave value evoked in isolation from one stimulus site (proximal or distal) does not localise the site of the lesion but merely indicates some alteration in the responsiveness of the anterior horn cell pool to antidromic volleys. This could result from a variety of lesions placed along the cord-muscle axis. By using two stimulation sites, one proximal and one distal to a segmental nerve lesion, a significant difference in the pattern of backfired late responses evoked by the distal, rather than the proximal, stimulus not only determines the presence of the lesion but also, the author believes, localises the lesion. The method offers a new approach to the detection and localisation of peripheral nerve lesions.

It should be noted that the absence of any muscular branch of the median nerve between the two sites of stimulation to the test motor axons is important. It might be expected that, in health, if additional axons fed into the mixed nerve between the two stimulation sites the proximal stimulus would result in a different pattern of Renshaw activity within the spinal cord (compared with the distal stimulus) and change the F-generating activity in the test motor neurone pool.

The speculation which prompted this study may be fortuitous and may not represent the underlying mechanism of these observations in the carpal tunnel syndrome group. The fall in F-wave persistence and the increase in %Repeater F-wave values evoked with the distal stimulus suggests that if the afferent volley traverses a damaged mixed peripheral nerve a smaller fraction of the total number of anterior horn cells in the test motor neurone

pool participate in generating F-responses and that certain motor neurones' liability to discharge a recurrent response is facilitated. As in some of the peripheral neuropathy cases described in 4.3, in some cases highly persistent Repeater F-waves were evoked by the stimulus distal to the lesion. When an electrical stimulus is applied proximal to the dysfunctioning nerve segment, the pattern of Renshaw inhibition in the motor neurone pool will be the same as in health. (This assumes that the stimulus is proximal to any segmental demyelination, in sensory and motor fibres, and that no axonal degeneration has taken place in the nerve). The inhibitory effect of the earliest antidromic impulses, seen in the healthy state, will therefore be unaffected by the lesion distal to the site of the stimulus. If the initial impulses reaching the ventral horn of the cord, via fastest conducting axons, have a repressive effect on other groups of motor neurones' discharging liability, this effect will be maintained. However, with the stimulus applied distal to the affected nerve segment the profile of the antidromic volley will be modified; both temporal dispersion and impulse blocking may occur. If large motor axons are most susceptible to damage in entrapment one can expect the earliest phase of Renshaw inhibition to be modified and this could, perhaps, result in derepression in some motor neurones or groups of motor neurones permitting them to discharge F-responses at increased levels of persistence.

Additional physiological disruption due to sensory fibre lesions should not be ignored. These factors have already been considered (see 4.3.4).

6.7 Carpal Tunnel Syndrome Mimicking Cervical Spondylosis - The Role of F-response Analysis in Differentiating the Two: An Experiment

6.7.1. Introduction

Signs and symptoms of cervical spondylosis and carpal tunnel syndrome overlap. In some cases, therefore, the absence of any pathognomonic clinical feature could result in diagnostic error. As both are commonly invoked diagnoses the opportunity for misdiagnosis is considerable.

A median nerve lesion in the carpal tunnel can come to light in a variety of ways, e.g. as a purely nocturnal sensory syndrome, as an activity related motor syndrome, as painless wasting of the thenar eminence, as an isolated patch of paraesthesiae on a single digit or as an incidental electrophysiological finding lacking any clinical correlate. The aetiology of some presentations is more readily identifiable than others. Reaching a correct clinical diagnosis of carpal tunnel syndrome poses little challenge when sensory splitting of the ring finger (an exceptionally uncommon sign or symptom) or Phalen's sign is present. Difficulties, however, frequently arise in the patient with non-specific symptoms of brachalgia with or without hand/forearm sensory symptoms in the C6 dermatome.

If carpal tunnel syndrome were to be mistaken for cervical spondylosis one would expect the error to be more prevalent in younger rather than older patients (e.g. less than 55 years of age). Personal observations, based on cases referred to Dundee Royal Infirmary's EMG Laboratory, suggest carpal tunnel syndrome is not infrequently misdiagnosed as cervical spondylosis by the referring clinician. The author regularly encounters patients in whom symptoms and signs could be apporpriate to either cervical spondylosis or carpal tunnel syndrome. This experiment derived from the

difficulties in reaching a definitive diagnosis in patients complaining of pain and/or disturbed sensation in the upper limb who exhibit no key diagnostic signs.

As F-wave abnormalities can be an isolated index of motor fibre dysfunction in a peripheral nerve entrapment syndrome (Shahani et al 1980(b)) and as motor fibre dysfunction may occur without sensory fibre dysfunction (Kimura 1979) F-wave measurements from abductor pollicis brevis, with its C8, T1 segmental representation (Goodgold 1974) might be a sensitive and quick test which could help to differentiate atypical carpal tunnel syndrome from cervical spondylosis in cases where symptoms are difficult to interpret, associated signs are lacking and where sensory and mixed nerve conduction studies of the median nerve were normal. The aims of this study were twofold: Firstly, to determine, using electrophysiological measurements of sensory and motor fibre function, the prevalence of median nerve dysfunction in a group of "young" patients diagnosed as having cervical spondylosis. Secondly, to determine the prevalence of median nerve F-wave conduction and F-discharge abnormalities. Motor conduction was measured in the distal segment (distal to the elbow) and proximal segment (proximal to the elbow) of the C8, T1 motor axons innervating abductor pollicis brevis in these patients diagnosed as suffering cervical spondylosis. This was done to see if a double-crush lesion of C8, T1 motor fibres could be identified in any of the cases.

6.7.2. Materials and methods

The author recruited a group of patients under the age of 55 years in whom the diagnosis of cervical spondylosis had been made more than two years prior to their entry into the study and did an electrophysiological and

clinical neurological assessment to determine the prevalence of median nerve dysfunction. "Young" patients (in terms of symptomatic cervical spondylosis) were examined as it was thought atypical carpal tunnel syndrome might be found more commonly in "younger" rather than "older" patients mistakenly diagnosed as having cervical spondylosis. The electrophysiological tests were additionally tailored to detect evidence of a double crush lesion (Eisen et al 1977(a)). While symptomatic spondylosis can be seen in patients in their fourth or fifth decades, it was felt that 55 years was an appropriate, although arbitrary, upper age limit for the study group.

Patients with a diagnosis of cervical spondylosis were found with the cooperation of the Orthopaedic Department at Bridge of Earn Hospital, Perthshire. Patients with a diagnosis made more than 24 months prior to the start of this study were culled from the outpatient clinic lists of three consultant surgeons from the year 1985. This allowed at least two years to pass since the original diagnosis in order that natural history of the complaint and the effects of treatment could be followed. These clinic lists identify each patient attending the clinic as having a "hand, elbow, neck, knee", etc., problem. The department does not keep a diagnostic register. I randomly selected 69 names of patients, under the age of 55, from those listed as having arm, neck or hand symptoms. Each of their records was scrutinised and from these 69 patients 27 patients were identified in whom a specialist had diagnosed cervical spondylosis. None had undergone electrophysiological assessments prior to the diagnosis of cervical spondylosis.

Findings of the specialists in 1985, at the time of diagnosis of cervical spondylosis, which were exclusion factors preventing acceptance into the study were: reduced arm reflexes or muscle wasting in the hand. Objective sensory loss, and restricted neck movement, were not exclusion factors. The X-ray appearances of the cervical spine, at the time of the

initial diagnosis, were not considered in selecting patients for the study. These 27 patients were contacted by letter and 7 (1 male, 6 female) volunteered to attend the EMG laboratory, Dundee Royal Infirmary, for electrophysiological tests and a clinical neurological examination. None suffered from a generalised neuropathy (no pedal symptoms, retained ankle reflexes), or any predisposition to such. Nine symptomatic arms were evaluated.

From each patient a history of the complaint was taken, and this included the evolution of symptoms since the initial diagnosis of cervical spondylosis was made. Each patient had a detailed neurological examination referrable to the nerve supply of the upper limbs and the long tracts to the lower limbs. The examination took particular note of two point discriminatory sense from each digit pulp and any areas of altered pinprick sensitivity were carefully recorded. Phalen's and Tinel's tests were used.

For the nerve conduction studies the forearm volar skin temperature was at or above 34°C. Recordings were made using a Medelec MS8 electromyograph. Paraspinal electromyography was performed with the patient decubitus and semi-prone with the neck comfortably supported and flexed, using a concentric needle electrode. Denervation potentials were sought using the 4 quadrant technique at four sites and motor units were not examined. F-waves were recorded from the motor point of the test muscles (abductor pollicis brevis and abductor digiti minimi) using a stimulus 20% greater than the voltage required to maximise the M wave. The %Repeater F-wave value was obtained from 100 F-waves sweeps photographed on a raster setting. The reader is referred back to 2.2.2. where the methodology for eliciting and recording F-responses, as it applies to this experiment, is described.

The proximal F-wave conduction velocity of the fastest motor axons innervating abductor pollicis brevis was calculated using the technique of measuring the distance (mm) from the C7 spinous process to the point of proximal stimulation (elbow) and dividing it by F-M-1/2 (ms) (where F and M represent minimal latencies of the F- and M waves evoked by the elbow stimulus) (Kimura 1974) (see 2.1.5). Sensory antidromic wrist-to-palm latency was measured over an 8 cm segment across the carpal tunnel (Kimura 1979).

Sensory conduction was measured through the medial and lateral antibrachial cutaneous nerves of the forearm to provide information on post-ganglionic sensory fibres traversing the medial and lateral cords of the brachial plexus respectively. Radial nerve orthodromic (digit 1) sensory potentials and median nerve antidromic potentials from digit 2 were measured as both derive from the fibres originating in the C6 dorsal root ganglia.

Eleven control subjects of similar age distribution (38-55 years) had proximal F-waves conduction velocities calculated (C7-elbow) bilaterally for purposes of comparison with the group of patients in this study. Further radiological assessments were not included in the study design.

6.7.3. Case Reports

Only positive examination findings (from the previous examination(s) in 1985, reported by the orthopaedic specialist, and the current examination) and points of interest are detailed. Unless mentioned, numb waking, a positive Tinel's sign and such features can be taken as absent.

Case 1 E.M. (07 04 35 (Tayside Health Board number), female) was referred five years ago by her practitioner with paraesthesiae in the right arm and hand (less but similar on the left) with intermittent neck stiffness and

posterior nuchlagia. She was thought then to have slight restriction of neck movement. Cervical spine X-ray showed C5-6, C6-7 disc space narrowing. A diagnosis of cervical spondylosis "with root pressure" was made. Tingling was noted "in the C6 distribution" (quoted from the Hospital record). The patient was hospitalised for cervical manipulation under general anaesthesia. Following this, and subsequent neck traction, no improvement was obtained.

Currently, symptoms persist in the dominant right hand alone. She experiences difficulty in threading a needle, picking up pins and she "fumbles" when turning the pages of a newspaper or book. Intermittent brachalgia over the outer aspect of the arm between wrist and mid upper arm occurs. There is numb tingling on the radial side of the hand.

There is now a reduction in pinprick sense over the dorsum of the index finger distal to the proximal interphalangeal joint.

Case 2 J.S. (19 11 37 (Tayside Health Board number), female) described the onset of right postero-lateral neck and shoulder pain, associated intermittently with daytime tingling of the pulps of the right index, middle, and ring fingers in 1983. At the onset there was a 6 month period of night waking but never with hand symptoms, only neck/shoulder pain. Then and now no signs wre found on examination. X-rays of cervical spine showed degenerative changes at C4-5 and C5-6 levels and cervical spondylosis was diagnosed.

Case 3 J.H. (07 08 57 (Tayside Health Board number), female) developed posterior nuchalgia in 1983, associated intermittently with aching of the left wrist and numbness of the left index finger. Then and now no signs were found on examination. X-rays of cervical spine showed C6-7 disc space

narrowing and cervical spondylosis was diagnosed.

Case 4 A.F. (18 05 36 (Tayside Health Board number), female) first experienced pain in both hands and forearms in 1984. Numbness was felt intermittently in all digits of both hands which were described as feeling "swollen". In 1985 some limitation of neck movement was found and cervical spine X-rays were normal. A diagnosis of cervical spondylosis was made.

Symptoms persist with occasional exacerbations. No localising signs were detected at this time. Numb waking has evolved since the diagnosis of cervical spondylosis was made.

Case 5 I.C. (12 06 39 (Tayside Health Board number), male). In 1982 this coffin maker was struck on the nape of his neck by a falling coffin. A 3 week period of self-limiting posterior nuchalgia followed. In 1985 the same trauma recurred. Some weeks after this he developed "cramps" in both arms and hands exacerbated by use of the hands. Since then he has had nocturnal waking with pain over the outer forearms and biceps muscles and numb tingling of both hands. For 2 years he has slept on the floor as he wakens less frequently than when in bed.

Then, and now there were no localising signs. Cervical spine X-ray in 1985 showed C6-7 disc narrowing. His symptoms were thought to be "typical of an exacerbation of cervical spondylosis".

His symptoms persist being predominantly nocturnal. He now describes the "flick sign". Occasionally there are work-related hand symptoms when the volar aspects of all his digits and both palms tingle and go numb up to the wrist. There have been no neck symptoms in the last 18 months.

Case 6 M.G. (01 10 47 (Tayside Health Board number), female). In 1976 there was discomfort in the right shoulder radiating into the ring and middle fingers which resolved spontaneously. In 1981 she had a whiplash cervical injury followed by transient neck and shoulder pain. Since 1985 there have been regular bouts of neck and bilateral upper arm pain.

Then (and now) there were no signs. Cervical spine X-rays showed C5-6 disc space narrowing. Cervical spondylosis was diagnosed.

Case 7 F.R. (08 09 44 (Tayside Health Board number), female). Symptoms started in 1984 with pain over the full length of right arm from fingers to shoulder. Paraesthesiae affected the whole of the right hand (not localised in any way) and were worse at night.

Examination (then and now) revealed no localising signs. X-rays of spine in 1985 showed incidental fusion of bodies of C2 and C3. She got no benefit from neck traction and has since had to give up her work.

She now demonstrates the "flick sign".

All cases were discharged from the Orthopaedic Clinic's follow-up service. (An important point).

6.7.4. Results

The results of nerve conduction studies and electromyography pertaining to median nerve function are listed in Table 29. The upper limit control value for the sensory antidromic wrist-palm latency measurement was 1.7. F-wave latencies are calculated to the nearest 0.5 ms. Of the 9 symptomatic upper limbs 6 had electrodiagnostic signs of median nerve fibre dysfunction, i.e. 4/7 of the cases with a diagnosis of cervical spondylosis. In one additional patient, Case 2 (J.S.), the sensory antidromic wrist-to-palm

TABLE 29

RESULTS OF NERVE CONDUCTION STUDIES RELEVANT TO MEDIAN NERVE FUNCTION AT CARPAL TUNNEL LEVEL

	TEST UPPER LIMB								
Nerve No. (Patient)	1(EM)	2(JS)	3(JH)	4(AF)	5(AF)	6(IC)	7(IC)	8(MG)	9(FR)
DISTAL MOTOR LATENCY M (ms)	3.7	3.1	3.0	7.0	7.0	2.9	2.9	3.1	4.2
MOTOR CONDUCTION VELOCITY (Forearm), M (m/s)	59.8	48.9	56.4	45.1	41.3	53.3	56.8	54.9	52.2
SENSORY ANTIDROMIC WRIST-PALM (8 cm) LATENCY: DIGIT II (ms)	2.1	1.8	1.6	A	A	1.5	1.6	1.6	3.6
PALM-WRIST MIXED NERVE CONDUCTION VELOCITY: M (m/s)	38.1	53.3	63.6	30.8	38.1	61.5	53.5	51.2	50.0
PALM-WRIST MIXED NERVE CONDUCTION VELOCITY: U (m/s)	61.5	54.2	57.1	66.6	66.7	60.8	57.1	58.5	61.5
ELECTROMYOGRAM: APB	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	D,DR
F-WAVE: MIN-MAX LATENCY: APB/M, WRIST STIMULUS (ms)	26-29	27-28	26-27	31-32	34.5-35.5	27-30.5	27.5-32.5	24-26	27-28
F-WAVE: MIN-MAX LATENCY: ADM/U, WRIST STIMULUS (ms)	26-28	28-29	25-26	22-23	22-23	25-27	25-27	25-27	23-25
% REPEATER F-WAVE VALUE	6	4	8	52	68	86	100	19	71

M = median nerve; U = ulnar nerve; APB = abductor pollicis brevis; ADM = abductor digiti minimi; SCV = sensory conduction velocity; D = denervation potentials; DR = decreased recruitment pattern; NAD = no abnormality detected; A = absent; IDI = first dorsal interosseous.

latency was borderline (1.8 ms) (upper value in control range 1.7 ms) but no evidence of motor fibre dysfunction was found. Of the 6 median nerves with clear cut abnormalities 4 had evidence of sensory fibre dysfunction while 2 (both from Case 5, I.C.) had only motor fibre dysfunction, evident solely in F-wave abnormalities: delayed, abnormally dispersed F-responses and abnormally high %Repeater F-wave values (for control reference range see 6.5.3). Electromyographic abnormalities were found in none of the paraspinal muscles tested and in only one abductor pollicis brevis muscle.

Electrophysiological results pertaining to a proposed spondylotic radicular lesion or "double crush" pathology are listed in Table 30. The fastest proximal segment (C7-elbow) F-wave conduction velocity (using the minimum F-wave latency) was invariably faster than the forearm segment motor nerve conduction velocity in the alpha motor axons of abductor pollicis brevis (as in the controls), and did not differ significantly from control values (mean 66.9 m/s, SD 5.8). No obvious abnormality of sensory amplitudes or obvious slowing of sensory conduction velocity was found in the medial or lateral antebrachial nerves of the forearm and no features suggestive of a brachial plexus/thoracic outlet lesion were identified (see 4.1.9).

6.7.5. Comments and conclusions

Electrophysiological signs of distal segment median nerve dysfunction have been found in 6/9 (66%) of the symptomatic arms tested. This is a high prevalence and can, to some extent, be explained by self selection. Those patients with persisting dysaesthetic symptoms (>2 years) which had progressed in severity and frequency could be expected to volunteer for further investigations. If, however, those 4 patients were the only ones in the initial random sample of 27 patients who had a median lesion the prevalence

TABLE 30

RESULTS OF NERVE CONDUCTION STUDIES AND ELECTROMYOGRAPHY RELEVANT TO C5/6 ROOT/PROXIMAL C8/T1 FUNCTION

	TEST UPPER LIMB								
Nerve No. (Patient)	1(EM)	2(JS)	3(JH)	4(AF)	5(AF)	6(IC)	7(IC)	8(MG)	9(FR)
SAP									
DIGIT V, ORTHODROMIC SCV (m/s)	52.2	51.5	52.8	57.1	52.6	58.8	56.9	52.2	58.2
DIGIT I ORTHODROMIC RADIAL SCV (m/s)	56.8	52.0	50.0	51.5	53.4	52.9	51.0	56.1	56.2
MEDIAL ANTEBRACHIAL CUTANEOUS NERVE, ORTHODROMIC SCV (m/s)	62.1	50.2	66.6	63.9	62.9	64.5	63.1	59.5	65.2
LATERAL ANTEBRACHIAL CUTANEOUS NERVE, ORTHODROMIC SCV (m/s)	58.7	47.8	54.3	61.3	59.6	62.4	61.1	58.7	72.0
F-WAVE: MIN-MAX LATENCY APB/M, WRIST STIMULUS (ms)	26-29	27-28	26-27	31-32	34.5-35.5	27-30.5	27.5-32.5	24-26	27-28
F-WAVE: MIN-MAX LATENCY ADM/U, WRIST STIMULUS (ms)	26-28	28-29	25-26	22-23	22-23	25-27	25-27	25-27	23-25
MOTOR CONDUCTION VELOCITY M, forearm (m/s)	59.8	48.9	56.4	45.1	41.3	53.3	56.8	54.9	52.2
F-WAVE CONDUCTION VELOCITY: C7-ELBOW, M. (m/s)	69.4	56.8	62.5	74.0	62.0	66.6	65.9	62.3	74.0
F-WAVE CONDUCTION VELOCITY: C7-ELBOW, U. (m/s)	68.2	62.1	66.0	69.0	72.0	65.5	64.0	64.8	71.5
ELECTROMYOGRAM: C5,C6,C7,C8									
PARASPINAL MUSCLES	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
I.D.I.	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD

would still be noteworthy (15%).

Of the 6 symptomatic limbs in which there was evidence of median nerve dysfunction, 5 had abnormalities of F-responses recorded from abductor pollicis brevis. In 2 limbs (I.C., I.C.) F-response abnormalities were the only abnormal electrodiagnostic findings. In both of these, proximal F-wave conduction velocity was within normal limits suggesting the F-wave latency abnormality originates in the distal segment of the median nerve. In one limb, (I., E.M.), in which there were delays in sensory and "mixed nerve" conduction the F-responses gave no evidence of an associated motor fibre lesion.

Difficulties arise in accurately ascribing a cause to the non-specific sensory symptoms in the hand/arm even with the finding of median nerve fibre dysfunction.

At the time these diagnoses of cervical spondylosis were made there were no pathognomonic clinical signs of carpal tunnel syndrome, and no signs of motor radiculopathy. The diagnosis of cervical spondylosis was, therefore, assumptive. The symptoms were not, presumably, suggestive enough of carpal tunnel syndrome to prompt evaluation with nerve conduction studies. It should be noted that the orthopaedic department from which these patients came refers a large number of patients to this EMG laboratory for pre-operative electrodiagnostic confirmation of carpal tunnel syndrome or for evaluation if the clinical diagnosis of carpal tunnel syndrome is in doubt; these cases did not raise that level of uncertainty.

Since 1985 when the diagnoses of cervical spondylosis were made, one case has developed the "flick sign" and 2 cases have developed numb waking with hand symptoms. In only one case (E.M.) hypalgesia has evolved in a distribution strongly suggestive of the median nerve territory, although it is still possible (but unlikely) that this area of hypalgesia represents a partial

lesion of the C6 sensory root. In all, 4 cases have developed features since 1985 which would raise the clinical suspicion of carpal tunnel syndrome and this is an important finding with relevance to the interpretation of the electrodiagnostic abnormalities (see below).

The possibility remains that 2 lesions coexist in these 6 upper limbs; median nerve entrapment and (presumably) C6 sensory radiculopathy. Postganglionic C6 sensory fibres were tested using the lateral antebrachial cutaneous nerve and the radial nerve sensory action potentials of the first digit; no abnormalities were seen. The sensory potentials' amplitudes were all within the laboratory's control range. The presence of a preganglionic C6 lesion has not been excluded, but in none has a reduction or loss of the biceps jerk evolved over a period of 2 or more years. Bilateral C6 sensory radiculopathy in two of the cases seems a most unlikely possibility, particularly as numb waking had developed in one, and in the other a predominantly nocturnal syndrome associated with the "flick" sign has persisted for several years. There was no evidence of a double crush lesion involving motor or sensory C8,T1 nerve fibres traversing the plexus or at an alternative site distal to the dorsal root ganglia. (The proximal F-wave conduction velocity was faster than forearm motor conduction velocity in all instances, as is usual in health) (see 2.1.5).

The symptoms in any of these 4 cases (6 limbs) found to have median nerve dysfunction cannot be ascribed with absolute reliability to either the putative cervical spondylotic lesion or the electrodiagnostic median nerve abnormality (although clinical features in some, now, suggest symptomatic median compression in the author's view). Patterns of pain and sensory disturbances beyond the median nerve's territory, e.g. affecting the forearm and the whole hand, do occur quite commonly in median nerve entrapment within the carpal tunnel and can be misleading when characteristic signs are

absent (i.e. classic presentations often have atypical elements which are usually ignored by the clinician as they do not fit in to the accepted concept of 'carpal tunnel syndrome'). The tendency to symptoms related to wrist usage in some of these cases is suggestive of median compression.

Case 2, in which proximal and distal upper limb symptoms were present, and associated with a borderline wrist-palm sensory latency, highlights some problems encountered in ascribing dysaesthetic, brachalgic sensory symptoms to one of two possible lesions, particularly when electrophysiological abnormalities are only subtle. Median nerve conduction study abnormalities could be irrelevant to at least some of the patients in this study, as sensory and motor fibre abnormalities often produce no symptoms (see 5.3).

Although the number of cases studied in this experiment is small, the findings provide some support for the contention that carpal tunnel syndrome and cervical spondylosis can be clinically indistinguishable. In view of the difficulties in making a definitive diagnosis in the absence of key clinical features, it is suggested that cervical spondylosis should not be diagnosed clinically in patients under the age of 55 without investigation by electrodiagnostic tests, as atypical carpal tunnel syndrome could be the cause. The avoidance of inappropriate therapies (see Case 1) for atypical carpal tunnel syndrome is an important consideration (see also 5.4). The unfortunate consequences of a failure to implement a simple effective remedy (Case 7) are worth consideration.

Perhaps a "trial" of surgical decompression of the carpal tunnel may be considered appropriate by some clinicians as the final arbiter when faced with the problems illustrated here. The author's own preference in patients in whom cervical spondylosis and carpal tunnel syndrome cannot be differentiated is to test the effect of a steroid injection (with splintage if

nocturnal symptoms are prominent) prior to "test" surgical decompression of the carpal tunnel or radiculography.

We have cases, with symptoms similar to those in this study, attending our EMG laboratory in whom there have been no hard clinical signs of radiculpathy but who have been submitted to radiculography. The radiculogram has suggested a lesion for which a cervical decompression has been performed. Subsequently the patient has not improved and has been referred for electrodiagnostic assessment and in some of these patients median nerve abnormalities are detectable. Such a case, which highlights this point, is described in 5.4.

Since isolated F-wave abnormalities through C8,T1 were identified in some of these symptomatic hands (as well as being associated with other nerve conduction study abnormalities in some) F-wave measurements would appear to be useful in the initial evaluation of patients with these non-specific symptoms. The interpretation of subtle electrophysiological signs in the presence of non-specific symptoms remains difficult, but the findings of disturbed motor impulse transmission through C8,T1 fibres can, at least, act as a pointer to a possibly relevant lesion in the median nerve in this type of clinical situation and prompt serious consideration as to the origin of such symptoms. It is worth remembering that all the patients who volunteered for this study had been discharged from hospital care once the suggested treatments were tried and had failed.

6.8. The "Thinker" Sign: A New Clinical Sign

Occasionally a patient's "insight" into his or her own complaint can mislead the doctor. Patients often have an explanation to offer for their symptoms and, not uncommonly, they preface the description of their symptoms with their own concept of its pathophysiology. (This can be turned to the physician's advantage in some circumstances, particularly when the aetiology of the complaint is less clear to the physician than to the patient).

The author has encountered several patients who have presented with hand and forearm symptoms which they related directly (and mistakenly) to neck posture. Discomfort and numb tingling were triggered, so the patient said, by holding the neck in extension. Not unreasonably, having noted the association of extension of the cervical spine with their symptoms they assumed a cause and effect relationship (relief was obtained in seconds or minutes by changing posture). In each case the patient had described this relationship to their general practitioner who X-rayed the cervical spine and referred the patient to the neurology clinic.

When asked to reproduce the symptoms each patient adopted the posture seen in Figure 40(a) or Figure 40(b). These patients had been unaware that, in assuming this posture, they were concomitantly performing Phalen's test or a reverse Phalen manoeuvre on themselves and that their symptoms were triggered, not by the extension of their cervical spine, but rather by the position in which the wrist was being held.

On formal testing both forced flexion and extension of the wrist reproduced the symptoms while the neck was held in a neutral position. Electrophysiological tests gave confirmation of a lession in both sensory and motor fibres of the median in the carpal tunnel.

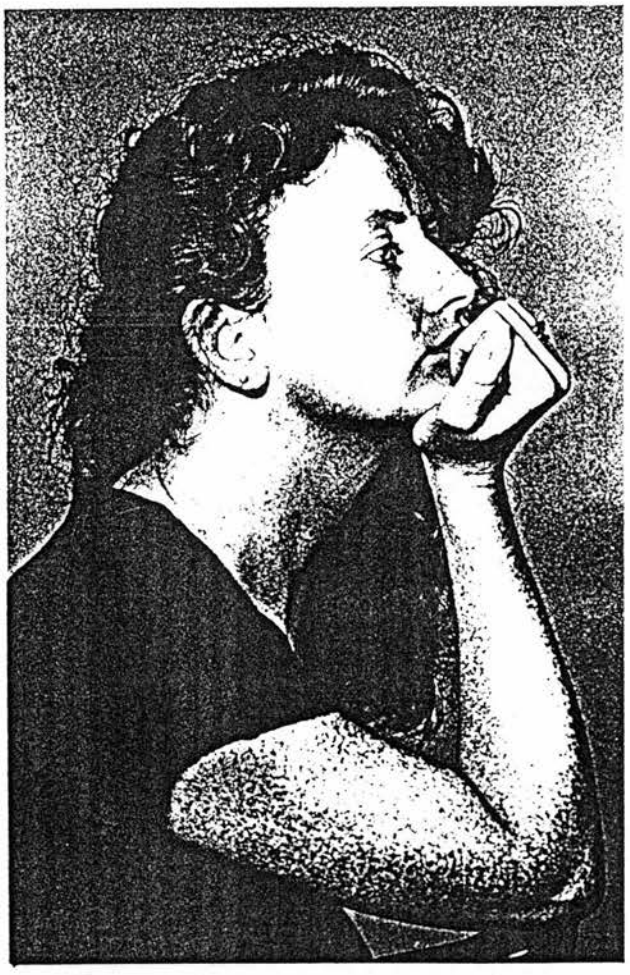


FIGURE 40(a)

THE "THINKER" SIGN

FIGURE 40(b)

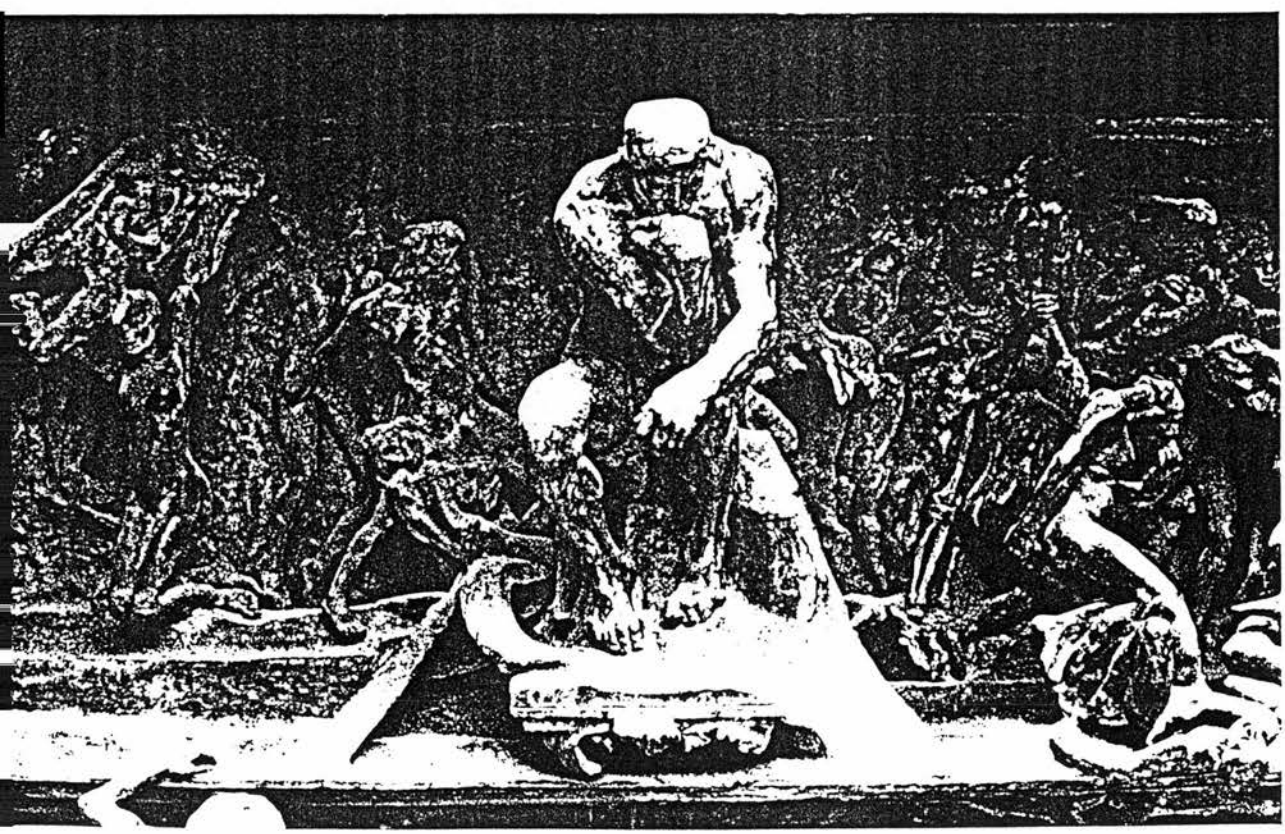
As this posture, with neck extended and wrist flexed or extended, tends to be assumed in times of deep contemplation it might reasonably be referred to as the "Thinker" sign (see Figure 41 A,B).

Patients relating arm and hand symptoms causally to neck posture can set their doctor off in the wrong direction in his attempt to localise a lesion. This sign might be remembered when the patient attributes pain and/or sensory symptoms in the arm or hand to neck extension, particularly when the pain and numb tingling induced are not localised to the median nerve's territory (see 6.7).

THE THINKER

FIGURE 41(a)

Rodin's statue "The Thinker" (initially conceived as "The Poet").



THE GATE OF HELL

FIGURE 41(b)

The source of contemplation

6.9. Motor Point Evoked F-waves in the Electrodiagnosis of Carpal Tunnel Syndrome: An Experiment

6.9.1. Introduction

In clinical neurophysiology F-responses are conventionally evoked by stimulating a mixed peripheral nerve with an electric shock. Difficulty in obtaining access to a muscle's nerve precludes the use of the F-response in the assessment of some of the more proximal limb muscles' nerves. One way of circumventing this difficulty would be to activate motor nerve fibres in the muscle at the motor point. This technique, if feasible, could provide an opportunity for the electrophysiologist to study conduction through nerve segments which cannot be tested by the conventional method.

There could be additional advantages to the technique. Nerve lesions might, theoretically, be more readily detected with the stimulus delivered at the most distal limit of the nerve trunk as this could permit maximisation of F-wave latency abnormalities (Lachman et al 1980).

As the percentage of the total motor unit population of a test muscle participating in the F-response after a single stimulus is very small, and because surface recordings can measure the onset of only the earliest conducted single unit F-response, it is possible, that if suitably positioned in the test muscle, a needle electrode with a restricted recording volume might have advantages over a surface electrode in detecting a greater range of conduction latencies for motor units participating in the F-response. The onset of individual motor unit components of the total F-response in a muscle, cannot be determined using a surface electrode unless there is gross F chronodispersion. The use of a needle electrode might allow slower conducted F-responses to be recorded selectively and allow a more sensitive measurement of true F chronodispersion, than the surface measurement of F

chronodispersion, which provides a latency measurement on only the fastest conducting motor units in each total muscle F-response in a sequence of F-responses.

This experiment is designed to answer 2 questions: Firstly, is it technically feasible to stimulate a muscle's motor point and record F-waves from that muscle with equipment available in an average EMG laboratory? Secondly, does stimulating motor axons distal (rather than proximal) to a lesion of the mixed nerve in this way, and recording the F-responses with a needle electrode, increase the electrodiagnostic yield in terms of F-response latency abnormalities?

These points have been studied by comparing the latencies of conventionally evoked/recorded F-responses with those of motor point evoked F-responses which have been recorded with a needle electrode from abductor pollicis brevis in a control sample and in a sample of patients with carpal tunnel syndrome.

6.9.2. Materials and methods

Patients in the study were all referred to the clinical neurophysiology laboratory at Dundee Royal Infirmary with a clinical diagnosis of carpal tunnel syndrome. None had a history of any condition other than carpal tunnel syndrome which might affect F-wave latencies through the median nerve nor had signs of any additional neural lesions. A physical examination was done to exclude, specifically, signs of myelopathy, radiculopathy and peripheral neuropathy. In each case the electrophysiological criterion for inclusion was prolongation of the sensory antidromic wrist-palm latency of the median nerve over 8 cm on the affected side (>1.8 ms) (Kimura 1979). A

diagrammatic representation of the method can be found in Figure 30, page 258. Thirty-two median nerves from 30 subjects with unilateral or bilateral carpal tunnel syndrome (17 female, 13 male, aged 30 to 66 years, mean 41 years) were studied. Only 2 patients with bilateral median dysfunction were studied due to the time it took to record F-responses at the various sites involved.

Thirty median nerves from 21 volunteers were used to obtain control values. Twelve volunteers were hospital staff, 4 attended the EMG laboratory for evaluation of isolated radicular symptoms in the leg/back pain, and 5 came to the neurology clinic with vascular headache. No test hands were affected by pain or neurological symptoms. No volunteer had, specifically, a past history of remitting neurological symptoms which could be construed as an episode of carpal tunnel syndrome. Each had a neurological examination which revealed no signs of nervous system disease (including those with back pain/sciatica). None had any identifiable predisposition to peripheral neuropathy (see 2.2.2) or peripheral nerve entrapment (previous wrist fracture, pregnancy or past history of teno-synovitis at the wrist). None of the subjects took neurotoxic medications (3 took Propranolol, one took Diazide, several used simple analgesics on a regular basis) and none were known to abuse alcohol. The only electro-physiological tests performed before admission to the study was a check of the median nerve's antidromic wrist-palm latency which had to be less than 1.7 msec over an 8 cm segment (Kimura 1979).

The volunteer subjects and patients were height matched: ranging from 5' 6" to 5' 8" (Conrad et al 1975, Weber and Piero 1978, Lachman et al 1980, Peioglou-Harmoussi et al 1985(a)). There was no statistically significant difference in the heights of the 2 groups at the 5% level.

F-waves were elicited in abductor pollicis brevis by stimulating at two sites; the median nerve at the wrist, just proximal to the transverse carpal ligament, and the muscle's motor point. The motor point was found by observing the site on the muscle's belly where the smallest intensity stimulus could elicit a muscle twitch. Bourguignon (1923) showed, in rabbits, by careful dissection, that the points over a muscle which were particularly sensitive to percutaneous electrical excitation were the points at which motor nerves dipped into the muscle just before fanning out. In this experiment the stimulator was hand-held. During the recording of F-responses the stimulator, (for type see 2.2), was orientated with its cathode placed proximally both for mixed nerve and motor point stimulation.

For each test limb the following protocol was observed: six individual motor point evoked F-responses were recorded from abductor pollicis brevis with a concentric needle electrode while the muscle was stimulated percutaneously with an electric shock delivered over the motor point. (The distance between the stimulating cathode and recording needle electrode was not standardised; they were Ca. 0.5 - 1.5 cm apart). Twenty F-responses were next recorded from the belly of abductor pollicis brevis with the same concentric needle electrode while the median nerve was excited 6 cm proximal to the motor point (just proximal to the distal skin crease at the wrist). Then, the needle electrode was removed and replaced with a surface disc electrode (silver/silver chloride 0.9 mm diameter), taped over the motor point of abductor pollicis brevis; 20 F-waves (>40 μV) were next recorded, by stimulating the median nerve at the wrist, 6 cm proximal to the site of stimulation previously used at the motor point. Finally, 20 F-waves (>40 μV) were recorded from abductor digiti minimi by stimulating the ulnar nerve 6 cm proximal to the site of the disc electrode on that muscle's motor point.

The cathodal stimulus point over the median nerve's trunk at the wrist was 6 cm distant from the recording electrode at the motor point in each test. F-waves evoked by stimulating the motor point were recorded using a concentric needle electrode inserted into abductor pollicis brevis close to the stimulating cathode. The temperature of the forearm was maintained at, or above, 34°C throughout the test. The stimulus voltage used at the wrist for both surface electrode and needle electrode recordings was 20% supra-maximal for the surface recorded M wave. The stimulus delivered to the motor point was of an intensity adequate to maximise the M amplitude (with a stimulus delivered to the median nerve at the wrist and recording with a surface electrode). When recording with a surface electrode the signal was amplified (bandpass 20 Hz to 2 KHz) and displayed using the Raster setting on the oscilloscope of a Medelec MS8. The bandpass was changed to 500 Hz - 10 KHz when recording with the concentric needle electrode (the same type in each test). Photographic records were made for subsequent analysis.

The gain and sweep speed of the oscilloscope were adjusted to allow clear visualisation of any "late" potential's initial deflection from the baseline and its configuration. During the examination each subject was supine and relaxed.

It was found that weak shocks applied over the motor point were sufficient to produce a visible twitch capable of generating F-responses of varying persistence from one test site to another. For the purposes of the experiment high intensity shocks were used to reduce the chance of axon reflexes being recorded (see 3.5). To be regarded as an F-response, evoked by the motor point stimulus, a potential had to have a short rise time (<1 ms), an amplitude greater than 100 μV (base to peak) and be recorded at least twice with the same latency and configuration. Figure 42 illustrates two individual types of F-response, recorded more than twice, from the same

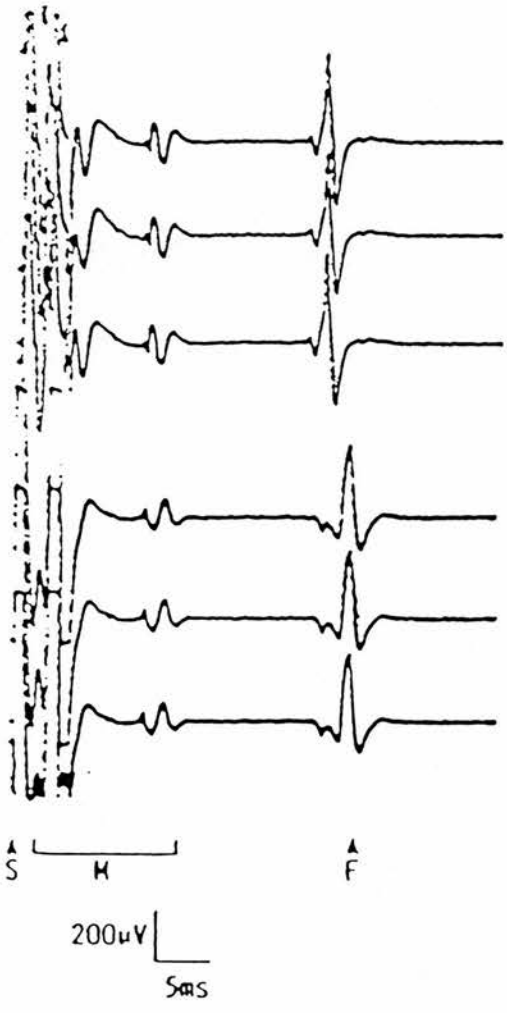


FIGURE 42

MOTOR POINT EVOKED F-RESPONSES

F-waves recorded from abductor pollicis brevis with a concentric needle electrode, while stimulating the motor point of that muscle.

: The upper 3 sweeps show an F-waveform recorded (and stored for photography) on 3 separate occasions. The F-wave has in each sweep an identical latency and configuration. 28 stimuli were used to record this potential x 3.

: The lower 3 sweeps show another F-response recorded from the same muscle after the recording electrode was moved very slightly (the delayed M component is still present, but now has a different configuration). 33 stimuli were needed to record the potential x 3.

In both instances a late M component precedes the F-response. When the lower 3 F-responses were being recorded the late M response appeared on the oscilloscope 33 times while the F-response appeared only 3 times.

test muscle using the concentric needle electrode. "Late" motor responses which appeared with each stimulus were taken to be M components (although there is the possibility of some being axon reflexes and were discarded from the analysis). Stimuli were delivered to both nerve and muscle at 1 Hz. The recording of 6 individual F-responses from each test abductor pollicis brevis muscle, while stimulating over the motor point, was accomplished fairly quickly in some instances, but in some cases was very time consuming and required several hundred pulses. In some hands, motor point evoked F-responses were highly persistent. Figure 43 shows 70 consecutive F-wave sweeps recorded with the needle electrode in which a highly persistent F-response appears.

For each test nerve/muscle four measurements were derived completely, or in part, from the latency data obtained from motor point evoked F-wave recordings: 1) the maximal latency of the motor point evoked F-waves (i.e. measured as the onset of the slowest conducted F-wave), 2) the latency range of the motor point evoked F-waves (i.e. the latency difference between the onset of the fastest and slowest conducted F-waves), 3) the latency difference between the onset of the earliest wrist evoked F-wave (of all F-responses recorded with both surface and needle electrodes) and the onset of the most slowly conducted motor point evoked F-wave, 4) the latency difference between the onset of the earliest wrist evoked F-wave (of all F-responses recorded with both surface and needle electrodes) and the onset of the most rapidly conducted motor point evoked F-wave.

The latency difference between the earliest wrist-evoked, surface recorded F-responses from abductor pollicis brevis and abductor digiti minimi was calculated from each test hand by stimulating over the trunk of the median and ulnar nerve at the wrist 6 cm proximal to the surface electrode, which was taped over the motor point of each test muscle.

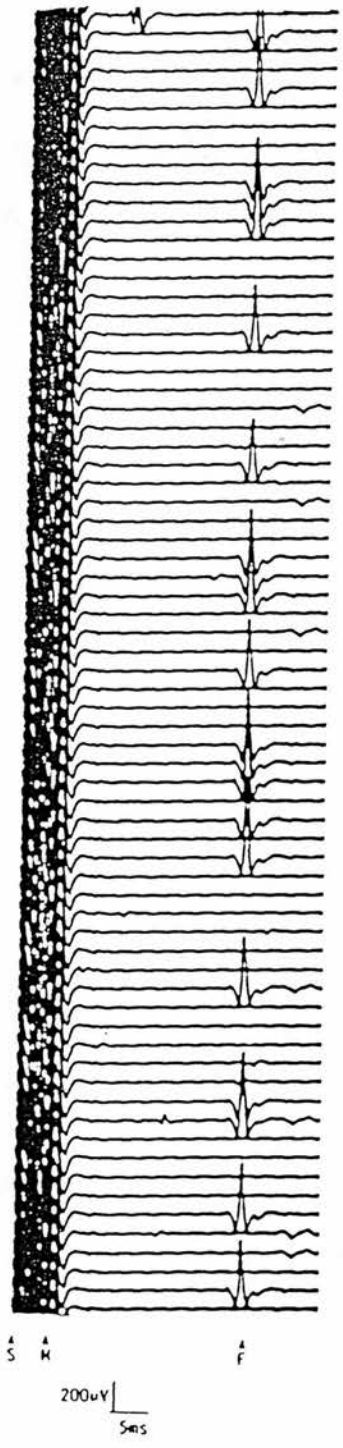


FIGURE 43

Motor point evoked F-responses recorded from abductor pollicis brevis in a patient with carpal tunnel syndrome.

A single, highly persistent, identical F-wave recurs at 34.5 msec.

6.9.3. Results

It was possible to record motor point evoked F-waves from each test muscle. Stimulus artefact was not a significant problem if the filter setting, described in the methods section, was used. In some cases, longer periods of stimulation were required to record an F-waveform for the second time, while in others, individual F-waveforms appeared with high levels of persistence.

It proved possible in several muscles to generate an identical M and F-response using a low intensity shock to the motor point. Figure 44 illustrates how the same potential can be recorded as an F- and M response. In sweep 4, using a weak shock, only an M response is recorded. Increasing the stimulus intensity slightly, in sweep 3, increases the complexity of the M wave. In this sweep the original M response is represented in the F-response and can be seen to be the initial component of the more complex M response. In sweep 2, while the stimulus intensity remains constant, the complex M response is retained but the single unit does not appear as an F-response. In sweep 1 the stimulus intensity has again been reduced to simplify the M wave to the single motor unit configuration seen in the fourth sweep and on this occasion it is followed by the same unit in the F-response. Thirty stimuli of a constant intensity had to be applied to obtain the same motor unit in the M and the F-responses pictured in sweep 1. In view of the impersistence of the single unit "late" motor response it is highly unlikely that the potential represents an axon reflex. On some occasions, components of the M response which were relatively delayed could be made to appear intermittently (as an F-response would) by moving the stimulator very slightly from side to side (see Figure 45). Late M components could be mistaken for F-responses, particularly if care is not taken to fix the relationship between the stimulus and the motor point. If low intensity

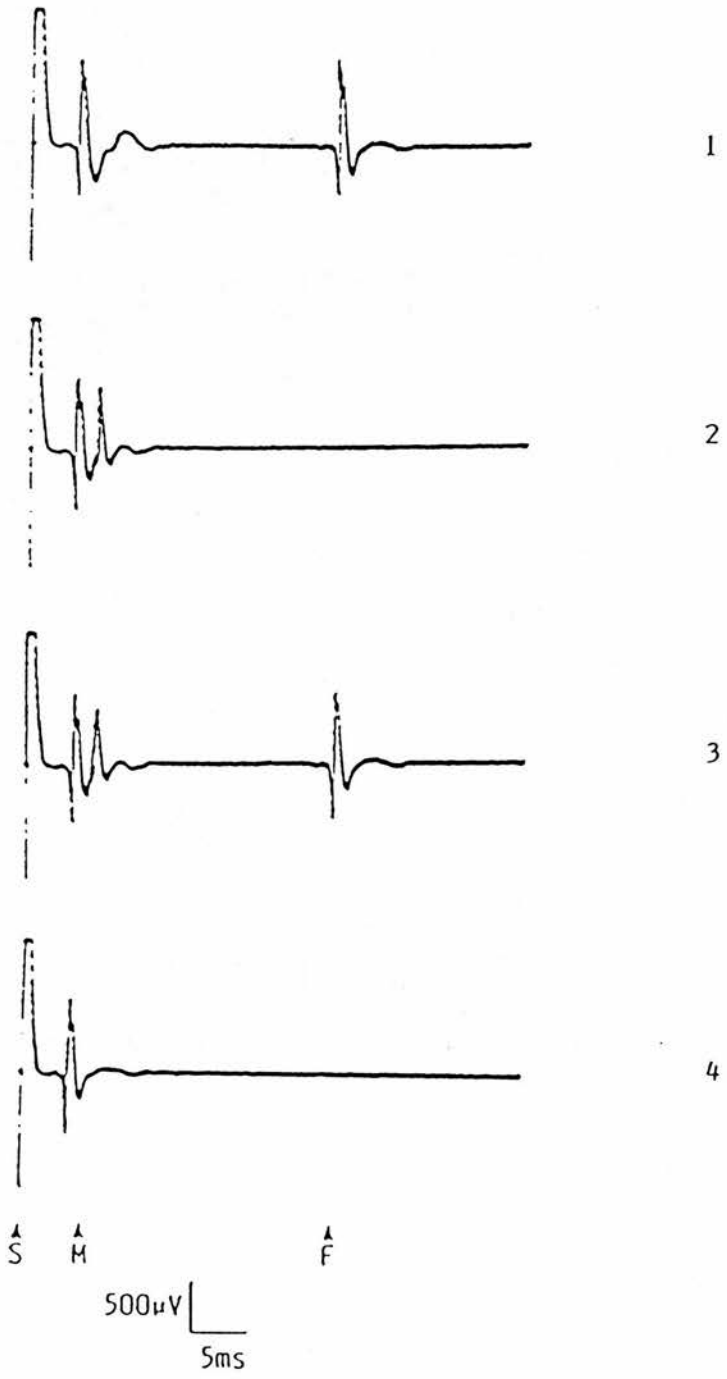


FIGURE 44

Motor point evoked M and F-responses from a healthy abductor pollicis brevis muscle. By adjusting the stimulus intensity the same muscle potential can be isolated in the M and F-response. In sweeps no. 1 and no. 4 stimuli of similar intensities activate a single motor unit directly. The same motor unit appears intermittently as an F-response (e.g. in sweep no. 1). When the M wave is more complex, as in sweeps nos. 2 and 3, the same unit can still be identified in the M and F-response.

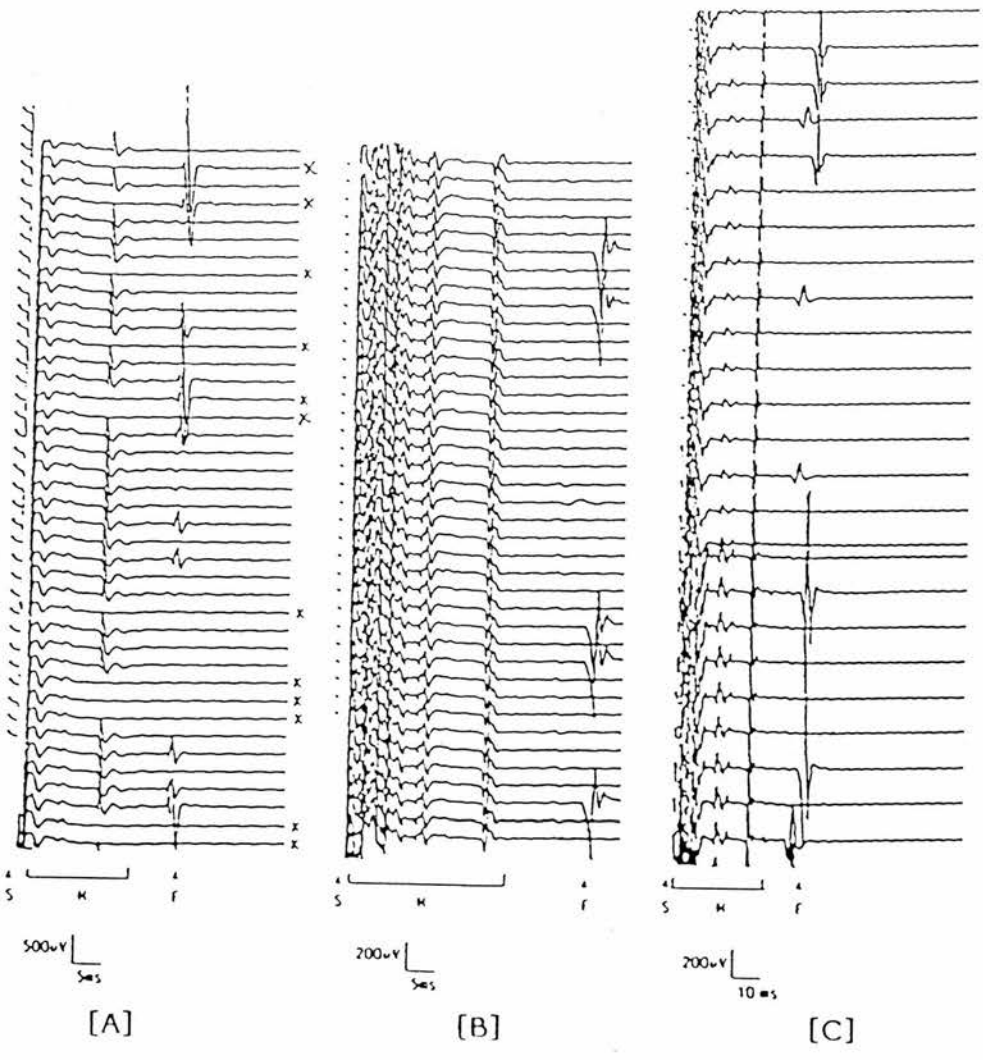


FIGURE 45

Motor point evoked M and F-waves from abductor digiti minimi and abductor pollicis brevis of a patient with carpal tunnel syndrome. F-wave sweeps are recorded using a concentric needle electrode inserted near the motor point of the muscle.

A: Normal latency F-responses from abductor digiti minimi (Ca. 28 ms) are preceded intermittently by a late M component (Ca. 16 ms). In each sweep marked X the stimulating electrode position has been adjusted slightly so that the late M response is abolished.

B: Delayed intermittent F-responses from abductor pollicis brevis (Ca. 43 ms), follow a late M component (Ca. 25 ms). (The M component follows each stimulus).

C: Delayed F-responses (3 F-waveforms appear twice or more), recorded from abductor pollicis brevis with a slight change in position of the recording needle electrode from that in B.

shocks were to be used, longer latency potentials could represent axon reflexes (see 3.5). These can be identified by observing the effect of maximising the stimulus intensity. In Figure 46 the first set of sweeps (no. 1) illustrates how a muscle potential appears in the F-response only if it present in the M wave (as in sweeps B and E). The stimulus intensity is maintained at a constant level in the sweeps pictured above sweep X (at 70 volts, 50 μs duration). In sweeps X and C stimulus intensity is reduced only very slightly and fails to excite a direct motor response. Long duration recordings (100 stimuli at 1 Hz) failed to yield a late muscle response with this stimulus just subliminal for the M wave. Even when a stronger stimulus is used, as in the lower sweeps, e.g. sweep B, the F-response appears impersistently. The second set of sweeps (no. 2) in Figure 46 illustrates the same principal. The same motor unit is activated directly and recurrently by a weak stimulus in sweeps A and D. In the majority of sweeps the potential is absent as an F-response, e.g. sweep B. When the stimulus intensity was reduced fractionally to abolish the M wave (e.g. sweep C) the unit never appeared as a late muscle response.

The motor point evoked responses in this study were elicited using a high intensity shock (100 μs duration and >200 V) to reduce the chances of recording axon reflexes, particularly in the carpal tunnel group.

Latencies of the F-waves recorded from abductor pollicis brevis muscles of the two test groups (carpal tunnel syndrome and control groups) are listed in Tables 31 and 32 respectively. In the control subjects, the mean difference between ulnar and median nerves' shortest latency F-responses (evoked from the wrist and surface recorded) in each limb was 1.1 ms (S.D. 0.6 ms). Of the 32 damaged median nerves tested, 14 had latency abnormalities of the conventional wrist evoked, surface recorded F-responses using the ulnar-median earliest F-waves' latency difference. All 14 had a

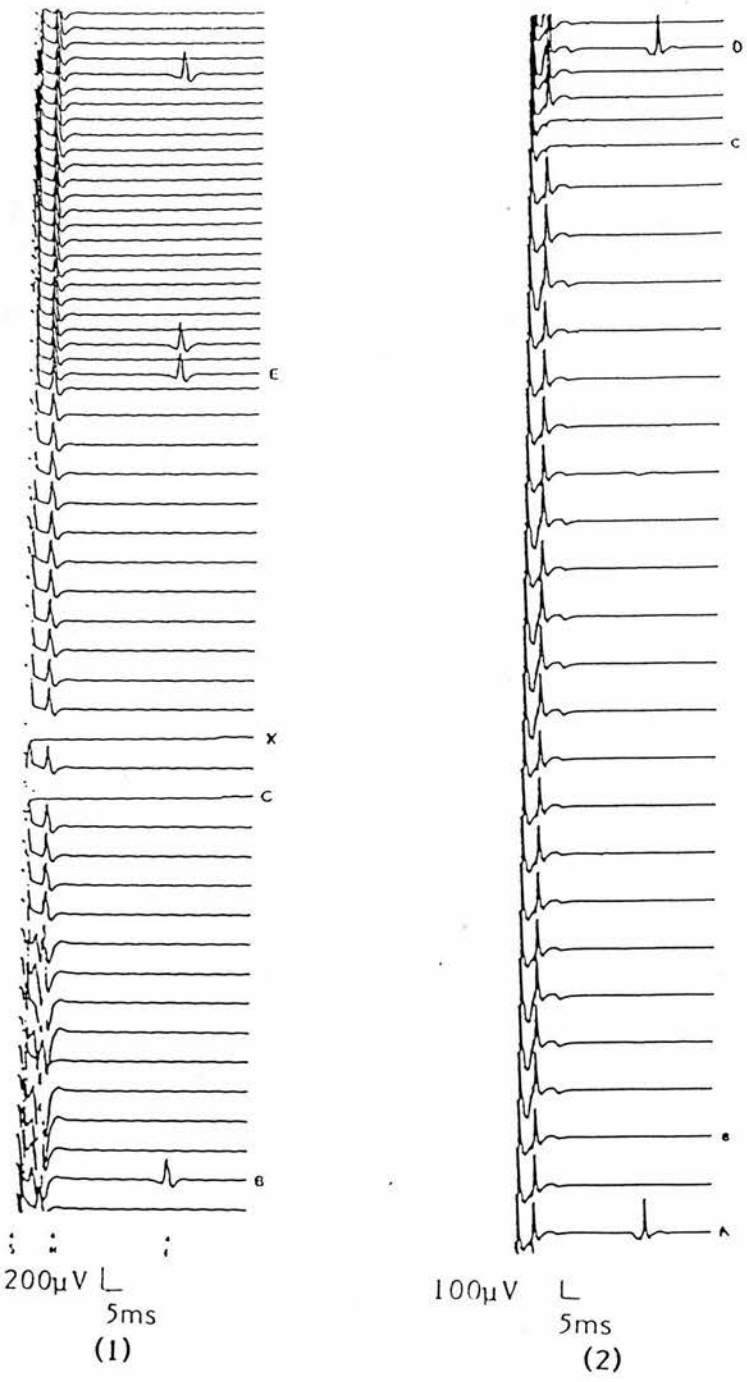


FIGURE 46

Motor point evoked F-waves recorded with a needle electrode from:

1: Adbuctor pollicis brevis,
2: Abductor digiti minimi

of a healthy volunteer.

TABLE 31

LATENCY DATA FROM THE MOTOR POINT EVOKED F-WAVE STUDY

CARPAL TUNNEL SYNDROME (n = 32)

Nerve No.	Wrist Evoked F-Wave Latency		Motor Point Evoked F-Wave Latency	Wrist Evoked F-Wave Latency
	Surface recording A.P.B.		Needle recording A.P.B.	Needle recording A.P.B.
	Minimum-maximum (ms)		Minimum-maximum (ms)	Minimum-maximum (ms)
1		25-26.5	28.5-30	25-28
2	XX	28.5-30.5	32-35.5	28-29
3	X XX	35-39	41-42	36-37
4	X XX	37-39	40-53	36-37
5	X XX	29-38	35-42	30-31
6	XX	29-31	35-38	28-29
7		25-27	30-33	26-27.5
8	X XX	33-37	43-48	33-36
9	X XX	28.5-32	34-37	29-31.5
10	X	28-29.5	31-35	27.5-29.5
11	XX	28-30	34-35.5	27.5-29.5
12	XX	28.5-30.5	34-40	29-31
13	XX	27-30	32-36.5	28-30
14	X XX	31-32.5	34-41	30.5-33
15	X XX	32.5-34.5	36.5-44.5	32-34
16	XX	26-29	31-36	28.5-30
17	XX	29-33	38-39	29.5-32.5
18	X XX	31-32	38-43	31-32
19	X XX	30-33.5	34-37	29-32
20	XX	29-32	35-38	29.5-34
21	X	29.5-35	31-35	29.5-34
22	XX	28-29.5	32-35.5	28-30
23	XX	25-27	31-31.5	25-27
24	XX	29.5-32.5	35-38	31-33
25	XX	28-30	30.5-36	27-28.5
26	X XX	37-39	48-48.5	39-39.5
27	X XX	34-38	38-43.5	35-39
28	XX	28.5-30.5	33.5-38	30-32.5
29	XX	27-29	32-41	27-30
30		28.5-31.5	30.5-34	28-31
31	X XX	28.5-32	37-41	29-32.5
32		27-29	30-32	27-27.5

Key: X = Conventional wrist evoked surface recorded F-wave latency abnormality
XX = Abnormal motor evoked F-wave latency parameter
APB = Abductor pollicis brevis

TABLE 32

LATENCY DATA FROM THE MOTOR POINT EVOKED F-WAVE STUDY

MEDIAN CONTROL NERVES (n = 30)

Nerve No.	Wrist Evoked F-Wave Latency	Motor Point Evoked F-Wave Latency	Wrist Evoked F-Wave Latency
	Surface recording A.P.B.	Needle recording A.P.B.	Needle recording A.P.B.
	Minimum-maximum (ms)	Minimum-maximum (ms)	Minimum-maximum (ms)
1	27-28	30-31	28-28.5
2	30-31.5	33-34	29.5-32
3	27-29	29-32	28-29
4	28-29	29-31	28-29
5	22-24	25-26	21-23
6	23-26	28-31	23.5-25.5
7	23.5-24.5	27-28	23-25
8	23.5-25	27.5-29	23-26
9	27.5-29	31-32	27.5-29.5
10	27.5-29	31-33	27.5-31
11	28-30	32-32.5	28-31
12	28.5-30.5	32-32.5	28-31
13	25.5-27	29-30.5	25-27
14	27-29	30-31	27-28
15	24-25.5	28.5-31.5	23-25
16	28-31	31-34	28.5-30.5
17	28-31	31-34	29-30.5
18	28-30	31.5-35	28-30
19	27-28	30-32	27-28
20	26-27	28-30	26.5-27.5
21	22-23	25.5-27	23-24
22	24.5-26.5	27.5-33	24-26
23	28-29.5	31-35	28-30
24	24-25	25.5-26.5	24-25.5
25	24-26	25-27.5	24-25.5
26	27.5-28.5	28.5-32	28-30
27	23.5-25	26-28.5	24-25.5
28	27.5-29	29.5-32	28-30
29	29-31	32-34	29.5-31.5
30	28-30	30.5-32.5	27.5-30

APB = abductor pollicis brevis

minimal latency abductor pollicis brevis F-wave at least 2.3 msec longer than the earliest F-wave recorded from that test limb's abductor digiti minimi, stimulating the ulnar nerve at the wrist.

The upper limit values of the four measurements derived from motor point F-wave recordings in the controls were as follows: 1) the maximal latency of the motor point evoked F-waves recorded was 35 ms. 2) the maximal latency range seen in an individual hand for the motor point evoked F-waves was 5.5 ms. 3) the maximal latency difference observed between the earliest wrist evoked F-wave and the latest motor point evoked F-wave was 9 ms, 4) the maximal latency difference observed between the earliest wrist evoked F-wave and the earliest motor point evoked F-wave was 5 ms.

To be regarded as an abnormal measurement, an observation (any of the four derived from motor point evoked F-waves) had to lie outside the range observed in the control subjects (this was decided in view of the relatively small numbers of observations made).

Twenty-six symptomatic hands had latency abnormalities derived from the motor point evoked F-waves. In 4 symptomatic hands no F-wave abnormality of any type was detected. Fourteen symptomatic hands were found to have conventional wrist evoked, surface recorded F-wave latency abnormalities (compared with the F-wave latencies of abductor digiti minimi in the same hand). Of those 14, 2 (no. 10 and 21) had no abnormality of the motor point derived F-response latencies. Fourteen symptomatic hands were found to have motor point evoked F-wave latency abnormalities, while the conventional F latency values (obtained from the wrist stimulus/surface electrode measurements alone) remained normal. In 3 of the 4 nerves in which F-wave latency parameters revealed no signs of motor fibre dysfunction there may have been no motor fibre dysfunction present or alternatively the tests were false-negative. In one case however, (no. 7),

electromyography revealed signs of denervation suggesting that the F-wave examination had failed to detect the motor fibre lesion.

Of the 4 measurements derived from motor point evoked F-responses the parameter which was most consistently abnormal was the value for the slowest conducted motor point evoked F-response. In 16 symptomatic hands the latency difference between the earliest wrist-evoked F-wave and the latest motor point evoked F-wave was found to be greater than that seen in the control group. In 6 hands the motor point evoked F-response latency range exceeded that seen in the control group (5.5 ms).

Of the 14 nerves with a motor point evoked F-wave latency abnormality but with normal conventional wrist-evoked, surface recorded F-response values: 4 had 1, 4 had 2, 6 had 3 and none had 4 abnormal motor point evoked F-wave parameters.

In those same 14 hands the motor point evoked F-wave parameter which was most consistently abnormal was the maximal motor point evoked F-wave latency value (93%). Only 14% had a motor point evoked F-wave latency range >5.5 ms (the control upper limit). Of the 4 nerves which had, in isolation, a single motor point evoked F-response parameter abnormality, nos. 2, 22 and 25 had prolongation of the maximal motor point evoked F-response latency and no. 23 had an abnormal latency difference between the earliest wrist-evoked and the earliest motor point evoked F-responses. Less than 50% of the nerves with normal conventional F-wave latency values had an abnormality of the latency difference between the earliest wrist evoked F-response and the earliest motor point evoked F-response.

It is seen that the needle electrode recordings of F-responses evoked from the wrist do not yield consistently greater F chronodispersion values than the recordings made with a surface electrode in either the control group or the carpal tunnel patients. In the carpal tunnel syndrome group the

needle recorded F-waves' F chronodispersion values were often smaller than those made with the surface electrode in the same individual.

In 9 hands affected by carpal tunnel syndrome an abductor pollicis brevis F chronodispersion value >3 ms (upper limit of control range) was observed, while 14 hands exhibited a delay in the conventional minimum latency F-wave recorded from abductor pollicis brevis compared with that of abductor digiti minimi. In some damaged nerves e.g. nos. 4 and 26 the earliest F-wave recorded conventionally from abductor pollicis brevis was grossly delayed (e.g. 37 ms) while the chronodispersion value remained within the normal range, e.g. 2 ms.

6.9.4. Comments and conclusions

In theory, F-responses elicited by a stimulus distal rather than proximal to a mixed peripheral nerve lesion are more likely to show latency abnormalities. Any prolongation of F-response latencies resulting from a stimulus delivered proximal to a dysfunctioning nerve segment will presumably result from the single transit of motor fibre impulses across the damaged segment. If, however, the electrical stimulus is applied distal to such a nerve lesion there will be at least two significant differences. Firstly, the motor impulses traverse the dysfunctioning axon segment twice, allowing accumulated delays to be maximised. Secondly, the composition of the antidromic motor volley (and orthodromic sensory volley) will be altered. Some fibres will be blocked and others will conduct more slowly. Effects of this type on the sensory volley have uncertain significance to the response of test motor neurones generating F-responses but it is likely that antidromic motor volleys from the two sites will have different effects on motor neurones' liabilities to issue an F-wave due to differing patterns of Renshaw cell activation. Other mechanisms which might be relevant have already been

mentioned in 2.4.3.

The use of a needle electrode, rather than a surface plate, to record the F-responses from abductor pollicis brevis, might be expected to increase the detection rate of the later onset F-responses whose take-off might be obscured by the action potentials of faster conducting motor units.

The maximal F chronodispersion value recorded from the 30 'healthy' abductor pollicis brevis muscles, using a surface electrode, was 3 ms and using a needle electrode was 3.5 ms (stimulating the median nerve at the wrist). This suggests that there is a very narrow latency range for the onset of recurrent motor activity in the test muscles.

F-responses in abductor pollicis brevis have been recorded elsewhere, by stimulating the thenar branch of the median nerve distal to the transverse carpal (Maccabee et al 1980). Stimulation in the palm could inadvertently activate the ulnar nerve's branch to adductor pollicis as well as the thenar branch of the median nerve to abductor pollicis brevis. F-responses arising in adductor pollicis can be readily recorded through the bulk of abductor pollicis brevis (see Figures 36 and 38, pages 295 and 302) and could result in ulnar F-responses being confused with median F-responses. While this would not affect the recording of delayed F-waves in the median nerve, minimal latencies could be misleadingly normal. By using a needle electrode clear identification of the origin of the F-response becomes possible and allows the differentiation of those arising from ulnar and median innervated thenar muscle.

The results of this experiment suggest that evoking F-responses from the motor point is a method of generating F-responses which might be applied usefully in a number of situations. The electrodiagnostic information in carpal tunnel syndrome appears to be significantly increased by stimulating distally and recording with a needle when compared with

conventional techniques. The placement of the stimulus distal to the site of maximal nerve damage would appear to be of prime importance. In cases where there is no sensory lesion, and no denervation is present in the nerve's muscles, F-response abnormalities may be the only electrodiagnostic finding and methods which might increase the sensitivity of tests using F-wave analysis would be useful. Normal wrist evoked F-wave latency measurements associated with abnormal motor point F-wave latencies help localise the dysfunction to the distal segment of the nerve. This is likely to be of some use in patients with atypical symptoms and an absence of abnormal electrophysiological findings. The technique has not yet been systematically extended beyond the contents of this experiment. However, delayed motor point evoked F-responses from patients with other conditions have been recorded. Figure 47 illustrates delayed motor point evoked F-waves from a patient in the acute phase of Guillain-Barre syndrome. There is a conduction block in the distal segment of the ulnar nerve evident by the size of the M wave recorded from abductor digiti minimi.

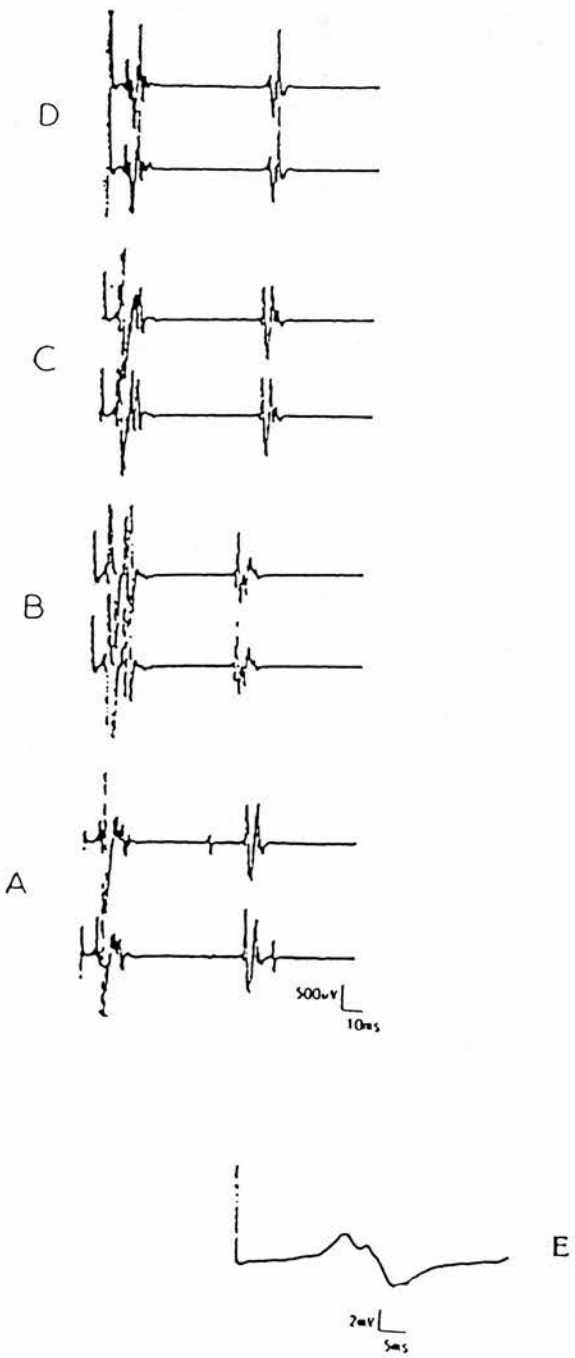
As a new technique for generating F-responses it opens up the possibility of recording F-responses from muscles whose nerve supply is inaccessible to surface stimulation, e.g. biceps, and may, importantly, offer a means of testing the proximal segments of the C5,6 roots which cannot, at present, be examined by conventional nerve conduction study techniques. By stimulating the motor point of different C5,6 innervated muscles it might prove possible to localise brachial plexus peripheral nerve and root lesions depending on the patterns of F-wave latency abnormalities detected.

Using measurements which incorporate F-wave latency values obtained by motor point stimulation the detection rate in the 32 entrapped nerves studied was 26 (81%) compared with 14 (44%) with conventional wrist evoked

FIGURE 47

Delayed motor point evoked F-waves from the abductor digiti minimi of a 27 year old with Guillain-Barré syndrome.

Using a concentric needle electrode, each F-wave, A, B, C, D, is recorded twice to confirm its latency and shape. E shows the small and delayed M wave evoked by a wrist stimulus and recorded by a surface electrode from the same muscle.



F-wave latency measurements.

The most prevalent motor point evoked F-wave abnormality was a delayed maximal latency value. The next most sensitive measurement was the latency difference between the earliest wrist evoked F-response and the latest motor point evoked response. In one nerve only the difference between earliest wrist evoked and earliest motor point evoked F-waves was outside the normal range and it therefore may be worth calculating this difference even if other parameters derived from motor point evoked responses are normal.

From the F chronodispersion values observed it seems unlikely that identification of the onset of F-responses which arrive at the muscle after the earliest transmitted F-response is contributing significantly to the sensitivity of this method. The finding of highly persistent F-responses in some hands affected by carpal tunnel syndrome, using this technique, is of interest. The single motor unit studies on F-wave persistence of Schiller and Stalberg (1978) used low intensity shocks which may generate patterns of F-wave persistence in single motor units different from those elicited by high intensity shocks. The author intends to investigate this finding.

For this technique to be applied in routine laboratory work larger numbers of control values would have to be determined.

6.10. Clinical Application of Motor Point Evoked F-responses: A Case Report

A case is presented to illustrate the way in which 2 of the new techniques for identifying median nerve dysfunction can provide evidence of a nerve lesion while conventional electrodiagnostic tests do not.

MR (Tayside Health Board no. 090643) a 44 year old 5' 4" female attended the Neurology Outpatient Clinic at Dundee Royal Infirmary with symptoms typical of carpal tunnel syndrome. These included numb waking and the unusual symptom of subjective sensory splitting of the ring finger (the only time the author has encountered a patient who volunteered the symptom). She described how the radial aspect of her ring finger was numb and tingled. The physical examination revealed that symptoms could be reproduced in the hand within 60 seconds by forced flexion of her wrist. Conventional nerve conduction study measurements (including distal motor latency, mixed nerve conduction velocity and sensory antidromic wrist-palm latency over the wrist-palm segment for the median nerve) were within the normal range. Ipsilateral ulnar and median nerve F-wave latencies (evoked at the wrist and recorded percutaneously from the hypothenar and thenar muscles, respectively) were 26-27.5 ms and 26-27 ms. The motor point evoked F-waves from abductor pollicis brevis had a maximal latency of 37 ms and this was attended by a %Repeater F-wave value of 59% obtained from a wrist stimulus to the median nerve, recording from abductor pollicis brevis. The patient was referred for surgery to decompress the carpal tunnel and obtained prompt relief.

There were 3 characteristic clinical features of median nerve compression in the carpal tunnel. (Sensory splitting of the ring finger, a positive Phalen's test and numb waking). Two of the new techniques using

F-response analysis gave results not seen in the control ranges described in 6.5 and 6.9. Interestingly, the F-response latencies and the F chrono-dispersion value obtained with a wrist stimulus were also normal.

The author believes that cases such as this show that the more recently introduced conventional tests of motor and sensory conduction still miss lesions of the median nerve.

6.11. An Economical Strategy for the Electrodiagnosis of Median Nerve Dysfunction in the Carpal Tunnel Syndrome

The new techniques using F-response analysis described in this thesis could have a supplementary role to the methods in conventional use (see 6.10). The author has found that the newer F-wave measurements can be isolated electrodiagnostic abnormalities (see 5.3, 6.10) and that they can be used to identify (6.5) and even accurately site (6.6, 6.9) lesions under the transverse carpal ligament. There is no reason to apply these techniques to patients who have lesions which are readily identified using conventional (more rapid, and less uncomfortable) tests.

The following protocol is suggested for the neurophysiological testing of a patient who might have carpal tunnel syndrome. The distal motor latency of the median nerve can be measured and at the same time, for quickness, F-wave latencies from abductor pollicis brevis can be determined. Some form of "trans-carpal tunnel" segment assessment can reasonably be done next (the author favours the "inching" sensory antidromic technique of Kimura and the comparison of mixed ulnar nerve and mixed median nerve conduction from palm to wrist). It is often helpful to test sensory antidromic conduction in the digital nerve fibres of not just the index finger but also of the middle finger, particularly if symptoms are present in that digit.

(The inclusion of motor conduction velocity measurement and a mixed nerve conduction velocity measurement for the forearm segment of the mean nerve is appropriate and the author likes to calculate the sensory conduction velocity in the palm to digit segment of the median nerve).

The normality, or otherwise, of F-wave latencies transmitted in the axons of abductor pollicis brevis can be ascertained in a number of different ways (see 6.2). The author uses the ipsilateral abductor digiti minimi F-wave latencies for comparison as well as the contralateral median F-waves from

abductor pollicis brevis and the F chronodispersion value for the F-responses from abductor pollicis brevis.

Should these tests reveal no evidence of nerve dysfunction it seems appropriate at this stage to analyse F-response patterns in abductor pollicis brevis. This can be done by stimulating the median nerve just proximal and then distal to the transverse carpal ligament. The %Repeater F-waves calculated from these two stimulation sites may reveal a lesion (see 6.6). If not, it is then appropriate when doing an electromyogram (which is very unlikely to reveal denervation if the other tests are normal) to calculate motor point-evoked F-response latencies (6.9).

RÉSUMÉ

Résumé of the main experimental findings

1) In the healthy human adult, F-wave production differs significantly in ipsisegmental motor neurone pools (C8/T1), as well as in motor neurone pools occupying different spinal segmental levels.
In health, the F-waves recorded from the surface of abductor pollicis brevis and abductor digiti minimi usually consist of persistent and variable waveforms while in extensor digitorum brevis F-wave impersistence associated with high Repeater F-wave counts are often found. In the intrinsic hand muscles tested, the F-wave persistence values were highly skewed (>75% of values were above 80). When identical F-responses (Repeater F-waves) were quantified using trains of 100 supramaximal stimuli, the vast majority of hand muscles yielded a count of less than 20. In extensor digitorum brevis, Repeater F-wave counts up to 71 were seen. There was a tendency to higher Repeater F-wave counts in abductor pollicis brevis than in abductor digiti minimi which just failed to reach significance at the 5% level.

2) A new measurement was devised to quantify F-wave production. It is designed to provide an index of the size of the subfraction of the test motor neurone pool which is active in generating F-waves across the full spectrum of F-wave persistence values. This measurement, the %Repeater F-wave value, was computed for 3 test motor neurone pools in health. Highly significant differences in values were found between small hand and foot muscles and differences were significant, at the 2% level, between values from 2 groups of different ipsisegmental intrinsic hand muscles.

3) The effect of age on F-wave persistence and on the %Repeater F-wave measurement was analysed in 2 groups of healthy volunteers. In the ulnar nerves/abductor digiti minimi muscles F-wave persistence and %Repeater F-wave values were not found to alter significantly with age.

In the median nerves/abductor pollicis brevis muscles, a significant age-related effect on the two measurements was found. F-wave persistence was found to be significantly less in the age groups ≤ 25 years, and >65 years, compared with the intermediate age groups and %Repeater F-wave values were significantly higher in the ≤ 25 year age group.

[The following findings apply only to median nerve/abductor pollicis brevis and/or ulnar nerve/abductor digiti minimi].

4) A variety of disorders which affect the peripheral nervous system (± central nervous system) were found to modify the F-wave generating behaviour of the motor neurone pools of abductor pollicis brevis and abductor digiti minimi. These disorders included Guillain-Barré syndrome, motor neurone disease, cubital tunnel syndrome, carpal tunnel syndrome, Charcot-Marie-Tooth syndrome, diabetic neuropathy and alcoholic neuropathy.

5) These disorders (as a group) resulted in the production of fewer F-waves with less variable waveforms than is seen in health.

6) Quantifying altered F-wave production in these disorders by measuring either F-wave persistence or the Repeater F-wave count alone can identify peripheral nervous system dysfunction but is very insensitive.

7) Disorders of the peripheral nervous system (e.g. cubital tunnel syndrome) can result in a pathological increase in persistence of Repeater F-waves.

8) Disorders of the peripheral nervous system can result in F-responses which occur "in series". "In series" Repeater F-waves were never encountered in the muscles of healthy volunteers.

9) The %Repeater F-wave value takes account of the observed effects of peripheral nervous system lesions on F-wave generators and can be used to identify lesions of the peripheral nervous system of different pathophysiological types (e.g. neuronopathy, demyelinating neuropathy and compression neuropathy). This measurement provides the basis of a new approach to the electrodiagnosis of peripheral nerve lesions.

10) The relationship between the M-wave's amplitude and the %Repeater F-wave value is not clear. It is often, but not always, inverse when the M wave is pathologically small. The relationship requires further study.

11) %Repeater F-wave values beyond those seen in the control reference range have been found in patients with peripheral nerve entrapment whose M wave amplitude remains in the control range.

12) The application of supramaximal shocks to record F-responses was only infrequently attended by an identical "late" response which followed each stimulus. Repeater F-waves did not display continuous persistence in the vast majority of the pathological material which was studied.

13) Intraspinal lesions (e.g. syringomyelia) can result in pathological ipsisegmental F-discharge patterns which can be identified by applying the %Repeater F-wave measurement.

14) In the course of a train of 1 Hz supramaximal shocks delivered to the median nerve, the responsiveness of the motor neurone pool of the test abductor pollicis brevis muscle is modified by the procedure. There is a systematic relative bias which results from the use of the first 30 of 100 F-wave sweeps (or the first 60 of 100) compared with the full set of 100 F-wave sweeps to calculate the %Repeater F-wave value. The relative bias associated with a 30 stimulus or 60 stimulus method provides an "underestimate" of the arbitrary "true" value obtained with a 100 stimulus method. Both in health and in the presence of a nerve lesion (motor neurone disease, carpal tunnel syndrome), the longer the test continues, the greater the % of obtained F-responses comprised of Repeater F-waves.

The imprecision of the method using 30 or 60 stimuli, was on a scale which had relevance to the application of the %Repeater F-wave measurement in the electrodiagnosis of peripheral nerve lesions.

The use of a 100 stimulus method to quantify a motor neurone's F-discharge pattern has advantages over methods which incorporate either 30 or 60 stimuli.

15) Abnormalities of F-response patterns can occur as isolated electrophysiological abnormalities. The use of the %Repeater F-wave value can allow the detection of some peripheral nerve lesions which are undetected by conventional nerve conduction studies.

16) An abnormal %Repeater F-wave value calculated from a train of stimuli delivered to a peripheral nerve at a single site does not localise the lesion along the axis of the test lower motor neurones.

17) F-discharge patterns from a motor neurone pool can be abnormal when stimuli are delivered proximal to a segmental lesion of the test mixed peripheral nerve (median nerve).

18) Conventional sensory, motor and "mixed" nerve conduction study parameters can remain within normal limits in the presence of longstanding (Ca. 2 years) symptomatic median nerve compression.

19) There is a high prevalence of electrophysiological abnormalities in the contralateral asymptomatic median nerves of patients with unilateral carpal tunnel syndrome.

20) Quantification of the production of F-waves by the motor neurones of abductor pollicis brevis offers a new and sensitive technique for the electrodiagnosis of median nerve compression in the carpal tunnel.

21) When a train of centripetal nerve volleys is set up in a damaged mixed peripheral nerve the observed pattern of F-discharging can be modified by moving the stimulus proximally so that additional motor and sensory impulses are included in the nerve volley which reaches the spinal cord.

22) In a group of median nerves damaged in the carpal tunnel, significant increases in F-wave impersistence ($p = 0.001$) and %Repeater F-wave values, measured from abductor pollicis brevis, resulted when the values were obtained with a stimulus moved from a site proximal to the carpal tunnel to a site distal to the carpal tunnel.

23) Eliciting F-responses with trains of stimuli proximal and distal to a segmental nerve lesion can allow, through measurement of the %Repeater F-wave value, not only the identification of a lesion of the mixed nerve, but also allow the position along the length of the test C8/T1 motor axons to be determined.

24) In some damaged median nerves, borderline %Repeater F-wave values measured with a wrist stimulus, became clearly pathological when the stimulus was delivered to the thenar branch of the median nerve.

25) F-wave persistence can increase, as well as decrease, in individual damaged median nerves when F-waves are elicited by a stimulus distal, rather than proximal, to the nerve lesion.

26) F-waves transmitted through the ulnar nerve can be recorded with a surface electrode over abductor pollicis brevis.

27) The recognition of median nerve dysfunction in the carpal tunnel can be difficult clinically.

28) Carpal tunnel syndrome is not uncommonly misdiagnosed as cervical spondylosis.

29) The interpretation of electrodiagnostic abnormalities of the median nerve is difficult when symptoms are nonspecific and atypical.

30) The F-wave provides a rapid and useful measurement which can be usefully applied to patients with nonspecific brachalgic/dysaesthetic arm or hand syndromes.

31) Awareness of the "Thinker" sign, particularly in patients with atypical carpal tunnel syndrome, could save unnecessary and inappropriate investigation in some instances.

32) F-waves can be elicited by stimulating the motor point of a skeletal muscle: A new method.

33) The use of motor point stimulation allows F-reponses to be recorded from a muscle whose motor nerve trunk is inaccessible to surface stimulation.

34) F-responses evoked from the motor point of abductor pollicis brevis permit an increase in sensitivity of F-wave latency measurements in the identification of median nerve motor fibre lesions in carpal tunnel syndrome, when compared with F-wave latencies derived from a wrist stimulus.

35) The most sensitive motor point evoked F-wave latency parameter for the identification of median nerve lesion in the carpal tunnel is the maximal motor point evoked F-wave latency value. Other motor point evoked F-wave latency parameters are also worth measuring if the maximal latency value is in the normal range.

36) Motor point evoked F-wave latency abnormalities may occur in isolation (i.e. are not accompanied by abnormalities on conventional nerve conduction studies) in some cases of carpal tunnel syndrome.

BIBLIOGRAPHY

Bibliography

ACKIL AA, SHAHANI BT, YOUNG RR.
Sural conduction studies and late responses in children undergoing haemodialysis (Abstract).
Archives of Physical Medicine and Rehabilitation 59, 562 (1978).

ACKIL AA, SHAHANI BT, YOUNG RR, RUBIN NE.
Usefulness of late response and sural conduction studies in patients with chronic renal failure (Abstract).
Electroencephalography and Clinical Neurophysiology 49, 20P (1980).

ADAMS RD, SHAHANI BT, YOUNG RR.
A severe pansensory familial neuropathy.
Transactions of the American Neurological Association 98, 67-69 (1973).

ADORNATO BT, GLASBERG MR.
Diseases of the spinal cord.
In: The Science and Practice of Clinical Medicine, Editor-in-Chief Dietschy JM, Grune and Stratton, New York (1980).

AIELLO I, SERRA G, MIGLIORE A, TUGNOLI V, ROCELLA P, CRISTOFORI MC, MANCA M.
Diagnostic use of H-reflex from vastus medialis muscle.
Electromyography and Clinical Neurophysiology 23, 159-166 (1983).

ALBIZZATI MG, BASSI S, PASSERINI D, CRESPI V.
F-wave velocity in motor neurone disease.
Acta Neurologica Scandinavica 54, 269-277 (1976).

ARGYROPOULOS CJ, PANAYIOTOPOULOS CP, SCARPALEZOS S.
F- and M-wave conduction velocity in amyotrophic lateral sclerosis.
Muscle and Nerve 1, 479-485 (1978).

ARVANITAKI A.
Effects evoked in an axon by activity of a contiguous one.
Journal of Neurophysiology 5, 89-108 (1942).

ASHBY P, WHITE DG.
"Presynaptic" inhibition in spasticity and the effect of β (4-chlorophenyl) Gaba.
Journal of the Neurological Sciences 20, 329-338 (1973).

ASBURY AK, ARNASON BG, ADAMS RD.
The inflammatory lesion in idiopathic polyneuritis: Its role in pathogenesis.
Medicine 48, 173-215 (1969).

BABA M, NARITA S, MATSUNAGA M.
F-wave conduction velocity from the spinal cord to the axilla without using collision technique. A simplified method.
Electromyography and Clinical Neurophysiology 20, 19-25, (1980).

BARAKAN TH, DOWNMAN CBB, ECCLES JC.
Electric potentials generated by antidromic volleys in quadriceps and hamstring motoneurones.
Journal of Neurophysiology 12, 393-424 (1949).

BERGER AR, SHAHANI BT.
Neurophysiologic evaluation of motor conduction in human spinal cords (Abstract).
Neurology 36 (Suppl 1), p.156 (1986).

BEYDOUN SR, ENGEL WK.
F-wave amplitude is rapidly increased in patients receiving intravenous or subcutaneous thyrotropin releasing hormone (T.R.H).
Neurology 35(Suppl. 1), p128 (1985).

BOLTON CF, GILBERT JJ, HAHN AF, SIBBALD WJ.
Polyneuropathy in critically ill patients.
Journal of Neurology, Neurosurgery and Psychiatry 47, 1223-1231 (1984).

BOLTON CF, LAVERTY DA, BROWD JD, WITT NJ, HAHN AF, SIBBALD WJ.
Critically ill polyneuorpathy: Electrophysiological studies and differentiation from Guillain-Barre syndrome.
Journal of Neurology, Neurosurgery and Psychiatry 49, 563-573 (1986).

BRADDOM RI, JOHNSON EW.
Standardisation of H-reflex and diagnostic use in S-1 radiculopathy.
Archives of Physical Medicine and Rehabilitation 55, 161-166 (1974).

BROWN TG.
On the nature of the fundamental activity of the nervous centres, together with an analysis of the rhythmic activity in progresion and a theory of the evolution of function in the nervous system.
Journal of Physiology (London) 48, 18-46 (1914).

BROWN WF.
A method for estimating the number of motor units in thenar muscles and the changes in the motor unit count with ageing.
Journal of Neurology, Neurosurgery and Psychiatry 35, 845-852 (1972).

BROWN WF, YATES SK.
Survival of lumbrical motor fibres in late-stage median nerve entrapments (Abstract).
Muscle and Nerve 3, 436 (1980).

BUCHTAL F, ERMINIO F, ROSENFALCK P.
Motor unit territory in different human muscles.
Acta Physiologica Scandinavica 45, 72-87 (1959).

BUCHTAL F, BEHSE F.
Peroneal muscular atrophy (PMA) and related disorders. 1. Clinical manifestations as related to biopsy findings, nerve conduction and electromyography.
Brain 100, 41-46 (1977).

BUCHTAL F, ROSENFALCK A, TROJABORG W.
Electrophysiological findings in entrapment of the median nerve at wrist and elbow.
Journal of Neurology, Neurosurgery and Psychiatry 37, 340-360 (1974).

CACCIA MR, McCOMAS AJ, UPTON ARM, BLOGG T.
Cutaneous reflexes in small muscles of the hand.
Journal of Neurology, Neurosurgery and Psychiatry 36, 960-977 (1973).

CAJAL RAMON YS.
Histologie du systeme nerveux de L'homme et des vertébrés.
A. Maloine, Paris, Vol. 1, p.986 (1909).

CAMPBELL MJ, McCOMAS AJ, PETITO F.
Physiological changes in ageing muscles.
Journal of Neurology, Neurosurgery and Psychiatry 36, 174-182 (1973).

CHOKROVERTY S.
Proximal nerve dysfunction in diabetic amyotrophy: An electrophysiological study (Abstract).
Electroencephalography and Clinical Neurophysiology 49, 20P (1980).

COËRS C.
Aspects histologiques de la régénération neuromusculaire au cours de diverses affections du neurone moteur périphérique; regeneration collaterale chez l'homme.
Acta Neurologica et Psychiatrica Belgica 55, 23-30 (1955).

C. PLINIUS SECUNDUS.
The Historie of the World. Commonly called The Naturall Historie of C. Plinius Secundus.
English Translation: by Philemon Holland, A. Islip: London (1601).

CONRAD B, ASCHOFF JC, FISCHLER M.
Der diagnostische wert der F-wellen-latenz
Journal of Neurology 210, 151-159 (1975).

DAUBE JR.
Percutaneous palmar median nerve stimulation for carpal tunnel syndrome (Abstract).
Electroencephalography and Clinical Neurophysiology 43, 139-140 (1977).

DAWSON GD.
The relative excitability and conduction velocity of sensory and motor nerve fibres in man.
Journal of Physiology (London) 131, 436-451 (1956).

DAWSON GD, SCOTT JW.
The recording of nerve action potentials through skin in man.
Journal of Neurology, Neurosurgery and Psychiatry 12, 259-267 (1949).

DAWSON GD, MERTON PA.
"Recurrent" discharges from motoneurones (Abstract).
20th International Congress of Physiology, Brussels: Résumés des Communications. p.221-222 (1956).

DEKEL S, COATES R.
Primary carpal stenosis as a cause of 'idiopathic' carpal tunnel syndrome.
Lancet 2, 1024 (1979).

DELWAIDE PJ.
Human monosynaptic reflexes and presynaptic inhibition.
In: New Developments in Electromyography and Clinical Neurophysiology, Vol. 3. Ed. Desmedt JE. Karger, Basel, pp.508-522 (1973).

DENNY-BROWN D.
Interpretation of the electromyogram.
Archives of Neurology and Psychiatry (Chicago) 61, 99-128 (1949).

DESCHUYTERE J, ROSELLE N.
Identification of certain E.M.G. patterns of the spinal cord reflexive activity in man. Electrophysiological study of discharges from spinal origin in the forearm flexors in normal adults.
Electromyography and Clinical Neurophysiology 14, 497-511 (1974).

DESCHUYTERE J, ROSELLE N, DE KEYSER C.
Monosynaptic reflexes in the superficial forearm flexors in man and their clinical significance.
Journal of Neurology, Neurosurgery and Psychiatry 39, 555-565 (1976).

DORFMAN LJ.
Indirect estimation of spinal cord conduction velocity in man.
Electroencephalography and Clinical Neurophysiology 42, 26-34 (1977).

DORFMAN LJ.
F-wave latency in the cervical rib-and-band syndrome.
Muscle and Nerve 2, 158-159 (1979).

DYCK PJ, LAIS AC, OFFORD KP.
The nature of myelinated nerve fibre degeneration in dominantly inherited hypertrophic neuropathy.
Mayo Clinic Proceedings 49, 34-39 (1974).

DYRO FM, ROSSIER AB, FOO DK.
F-wave measurements in post-traumatic syringomyelia (Abstract).
Muscle and Nerve 6, 526 (1983).

ECCLES JC.
The central action of antidromic impulses in motor nerve fibres.
Pflügers Archiv fur die Gesamte Physiologie des Menschen und der Tiere (Bonn) 260, 385-415 (1955).

ECCLES JC, SHERRINGTON CS
Numbers and contraction-values of individual motor units examined in some muscles of the limb.
Proceedings of the Royal Society, London, 106, 326-357 (1930).

ECCLES JC, SHERRINGTON C.
Studies on the flexor reflex. III. The central effects produced by an antidromic volley.
Proceedings of the Royal Society (London) B107, 551-605 (1931).

ECCLES JC, RALL W.
Effects induced in a monosynaptic reflex path by its activation.
Journal of Neurophysiology 14, 353-376 (1951).

ECCLES JC, ECCLES RM, IGGO A, ITO M.
Distribution of recurrent inhibition among motoneurones.
Journal of Physiology (London) 159, 479-499 (1961).

EDDS MV, Jr.
Collateral nerve regeneration.
Quarterly Review of Biology (Baltimore) 28, 260-276 (1953).

EDITORIAL.
Diagnosis of the carpal tunnel syndrome.
Lancet 1, 854-855 (1985).

EGLOFF-BAER S, SHAHANI BT, YOUNG RR.
Usefulness of late response studies in diagnosis of entrapment neuropathies (Abstract).
Electroencephalography and Clinical Neurophysiology 45, 16P (1978).

EICHLER W.
Über die ableitung der aktionspotentiale vom menschlichen nerven in situ.
Zeitschrift für Biologie 98, 182-214 (1937).

EISEN A, NUDELMAN K.
Cord to cortex conduction in multiple sclerosis.
Neurology 29, 189-193 (1979).

EISEN A, ODUSOTE K.
Amplitude of the F wave: A potential means of documenting spasticity.
Neurology 29, 1306-1309 (1979).

EISEN A, SCHOMER D, MELMED C.
The application of F-wave measurements in the differentiation of proximal and distal upper limb entrapments.
Neurology 27, 662-668 (1977(a)).

EISEN A, SCHOMER D, MELMED C.
An electrophysiological method for examining lumbosacral root compression.
Le Journal Canadien des Sciences Neurologiques 4, 117-123 (1977(b)).

EISEN A, BURTON K, LARSEN A, HOIRCH M, CALNE D.
A new indirect method for measuring spinal conduction velocity in man.
Electroencephalography and Clinical Neurophysiology 59, 204-213 (1984).

EKLUND G.
A new electrodiagnostic procedure for measuring sensory nerve conduction across the carpal tunnel.
Journal of Medical Sciences (Upsala) 80, 63-64 (1975).

EKSTEDT J, HÄGGQUIST P, STÅLBERG E.
The construction of needle multi electrodes for single fibre electromyography.
Electroencephalography and Clinical Neurophysiology 27, 540-543 (1969).

ELIZAN TS, SPIRE JP, ANDIMAN RM, BAUGHMAN FA, LLOYD SMITH DL.
Syndrome of acute idiopathic ophthalmoplegia with ataxia and areflexia.
Neurology 21, 281-292 (1971).

ENGEL WK, SIDDIQUE T, NICOLOFF JT.
Effect on weakness and spasticity in amyotrophic lateral sclerosis of thyrotropin-releasing hormone.
Lancet 2, 73-75 (1983)

ERTEKIN C.
Sensory and motor conduction in motor neurone disease.
Acta Neurologica Scandinavica 43, 499-512 (1967).

ESTEBAN A.
Neurophysiological study of a radiation-induced brachial plexus neuropathy (Abstract).
Electroencephalography and Clinical Neurophysiology 64, 2P-3P (1986).

FEASBY TE, BROWN WF.
Variations of motor unit size in the human extensor digitorum brevis and thenar muscles.
Journal of Neurology and Neurological Sciences 37, 916-926 (1974).

FETZ EE, JANKOWSKA E, JOHANNISSON T, LIPSKI J.
Autogenetic inhibition of motoneurones by impulses in Ia muscle spindle afferents.
Journal of Physiology (London) 293, 173-195 (1979).

FISHER CM.
An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia ataxia and areflexia).
New England Journal of Medicine 255, 57-65 (1956).

FISHER MA.
Electrophysiological appraisal of relative segmental motoneurone pool excitability in flexor and extensor muscles.
Journal of Neurology, Neurosurgery and Psychiatry 41, 624-629 (1978).

FISHER MA.
F-waves: Comments on the central control of recurrent discharges (Letter).
Muscle and Nerve 2, 406 (1979).

FISHER MA.
F-response latency determination.
Muscle and Nerve 5, 730-734 (1982).

FISHER MA, SHAHANI BT, YOUNG RR.
Assessing segmental excitability after acute rostral lesions. I. The F response.
Neurology 28, 1265-1271 (1978(a)).

FISHER MA, SHIVDE AJ, TEIXERA C, GRAINER LS.
Clinical and electrophysiological appraisal of the significance of radicular injury in back pain.
Journal of Neurology, Neurosurgery and Psychiatry 41, 303-306 (1978(b)).

FORBES A, SMITH OC, LAMBERT EF, CAVENESS WF, DERBYSHIRE AJ.
Central inhibitory mechanism investigated by means of antidromic impulses.
American Journal of Physiology 103, 131-142 (1933).

FOX JE, HITCHCOCK ER.
Changes in F wave size following dorsal root section (Abstract).
Electroencephalography and Clinical Neurophysiology 61, S.62 (1985).

FRA L, BRIGNOLIO F.
F and H responses elicited from muscles of the lower limb in normal subjects.
Journal of Neurological Sciences 7, 251-261 (1968).

FULLERTON PM, GILLIATT RW.
Axon reflexes in human motor nerve fibres.
Journal of Neurology, Neurosurgery and Psychiatry 28, 1-11 (1965).

GALVANI L.
De viribus electricitatis in motu musculari commentarius (1792).
Translation by GREEN R.
Commentary on the effect of electricity on muscular motion.
Elizabeth Licht: Cambridge, Massachusetts, USA (1953).

GARCIA-MULLIN R, MAYER RF.
H reflexes in acute and chronic hemiplegia.
Brain 95, 559-572 (1972).

GASSEL MM, TROJABORG W.
Clinical and electrophysiological study of the pattern of conduction times in the distribution of the sciatic nerve.
Journal of Neurology, Neurosurgery and Psychiatry 27, 351-357 (1964).

GASSEL MM, OTT KH.
Local sign and late effects on motoneuron excitability of cutaneous stimulation in man.
Brain 93, 95-107 (1970).

GASSEL MM, MARCHIAFAVA PL, POMPEIANO O.
Modulation of the recurrent discharge of alpha motoneurones in decerebrate and spinal cats.
Archives Italiennes de Biologie (Pisa) 103, 1-24 (1965).

GILBERT RW, KIM JH, POSNER JB.
Epidural spinal cord compression from metastatic tumor: Diagnosis and treatment.
Annals of Neurology 3, 40-51 (1978).

GILBERT W.
De Magnete, Magnetisque Corporibus, et de Magno Magnete Tellure; Physiologia nova, plurimis et argumentis, et experimentis demonstrata. Excudebat Petrus Short: London, 1600.
Translation: MOTTELAY P. FLEURY. William Gilbert of Colchester . . . On the loadstone and magnetic bodies and on the great magnet the Earth. A new physiology, demonstrated with many arguments and experiments. Bernard Quaritch: London (1893).

GILLIATT RW.
Axon branching in motor nerves.
In: B.L Andrew (Ed). Control and Innervation of Skeletal Muscle. Livingstone, Edinburgh, pp.53-63 (1966).

GILLIATT RW, HARRISON MJG.
Nerve compression and entrapment.
In: Peripheral Nerve Disorders. Ed. Asbury AK, Gilliatt RW. Butterworths: Bodmin. p.247 (1984).

GILLIATT RW, SEARS TA.
Sensory nerve action potentials in patients with peripheral nerve lesions.
Journal of Neurology, Neurosurgery and Psychiatry 21, 109-118 (1958).

GILLIATT RW, LE QUESNE PM, LOGUE V, SUMNER AJ.
Wasting of the hand associated with a cervical rib or band.
Journal of Neurology, Neurosurgery and Psychiatry 33, 615-624 (1970).

GILLIATT RW, WILLISON RG, DIETZ V, WILLIAMS IR.
Peripheral nerve conduction in patients with a cervical rib and band.
Annals of Neurology 4, 124-129 (1978).

GILLIES JD, LANCE JW, NEILSON PD, TASSINARI CA.
Presynaptic inhibition of the monosynaptic reflex by vibration.
Journal of Physiology (London) 205, 329-339 (1969).

GLASER J-S.
Myasthenic pseudo-internuclear ophthalmoplegia.
Archives of Ophthalmology 75, 363-366 (1966).

GLISSON F.
Tractatus de ventriculo et intestinis. Cui praemittitu alius, de partibus continentibus in genere, et in specie de iis abdominis.
London (1677).

GODAUX E, DESMEDT JE.
Human masseter muscle: H- and tendon reflexes. Their paradoxical potentiation by muscle vibration.
Archives of Neurology (Paris) 32, 229-234 (1975).

GOODGOLD J.
Anatomical Correlates of Clinical Electromyography.
The Williams and Wilkins Company, Baltimore, p65-67 (1974).

GRUNNET M, LUBOW M.
Ascending polyneuritis and ophthalmoplegia.
American Journal of Ophthalmology 74, 1155-1160 (1972).

GUILOFF MJ.
Peripheral nerve conduction in Miller Fisher syndrome.
Journal of Neurology, Neurosurgery and Psychiatry 40, 801-807 (1977).

HAGBARTH KE.
Post-tetanic potentiation of myotatic reflexes in man.
Journal of Neurology, Neurosurgery and Psychiatry 25, 1-10 (1962).

HAGBARTH KE, EKLUND G.
Motor effects of vibratory stimuli in man.
In: Muscular Afferents and Motor Control. Ed. Granit R. Almquist & Wiksell, Stockholm, pp.177-186 (1966).

HALLER A. VON.
Memoires sur la Nature Sensible et Irritable des Parties du Corp Animal.
Lausanne (1756).
Translation: A dissertation on the sensible and irritable parts of animals.
Introduction by Owsei Temkin. Johns Hopkins Press, Baltimore (1936).

HALTER SK, DeLISA JA, STOLOV WC, SCARDAPANE D, SHERRARD DJ.
Carpal tunnel syndrome in chronic renal dialysis patients (Abstract).
Muscle and Nerve 3, 438 (1980).

HAMILTON J.
Account of a trial of acupuncture with galvanism made by Dr W. Stokes one of the physicians to the Meath Hospital.
Dublin Journal of Medical and Chemical Science 6, 78-86 (1835).

HANSEN S, BALLANTYNE JP.
A quantitative electrophysiological study of motor neurone disease.
Journal of Neurology, Neurosurgery and Psychiatry 41, 773-783 (1978).

HAUSMANOWA-PETRUSEWICZ I, KOPEC J.
Motor nerve conduction velocity in lesions of the anterior horns.
In: Kakulas BA (Ed), Clinical Studies in Myology, Part 2.
Excerpta Medica, Amsterdam, pp.358-364 (1973).

HAYMAKER W, WOODHALL B.
Peripheral Nerve Injuries.
W.B. Saunders & Co., Philadelphia (1956).

HELMHOLTZ H VON.
"Messungen über den zeitlichen Verlauf der Zuckung animalischer Muskeln und die Fortpflanzungsgeschwindigkeit der Reizung in den Nerven."
Archiv für Anatomie, Physiologie und Wissenschaftliche Medicin 276-364 (1850).

HENNEMANN E, SOMJEN G, CARPENTER DO.
Functional significance of cell size in spinal motoneurones.
Journal of Neurophysiology 28, 560-580 (1965).

HODES R, GRIBETZ I.
H-reflexes in normal human infants: depression of these electrically induced reflexes in sleep.
Proceedings of the Society for Experimental Biology (New York) 110, 577-580 (1962).

HODES R, LARRABEE MG, GERMAN W.J.
The human electromyogram in response to nerve stimulation and conduction velocity of motor axons: studies on normal and on injured peripheral nerves.
Archives of Neurology and Psychiatry (Chicago) 60, 340-365 (1948).

HOFFMANN P.
"Über die Beziehungen der Sehnenreflexe zur willkurlichen Bewegung und zum Tonus."
Zeitschrift für Biologie 68, 351-370 (1918).

HOHMANN TC, GOODGOLD J.
A study of abnormal reflex patterns in spasticity. A new application of electrodiagnosis.
American Journal of Physical Medicine 40 52-55 (1961).

HUGHES JR, MORRELL RM.
Post-tetanic changes in the human neuromuscular system.
Journal of Applied Physiology 11, 51-57 (1957).

HUMPHREY JG.
Motor nerve conduction studies in the Landry-Guillain-Barre syndrome. (Acute ascending polyneuropathy) (Abstract).
Electroencephalography and Clinical Neurophysiology 17, 96 (1964).

ILES JF.
Responses in human pretibial muscles to sudden stretch and to nerve stimulation.
Experimental Brain Research 30, 451-470 (1977).

IOKU M.
Hand H-reflex demonstrated in patients with central nervous system disorders.
Electromyography and Clinical Neurophysiology 24, 331-339 (1984).

JABRE JF.
Ulnar nerve lesions at the wrist: New technique for recording from the sensory dorsal branch of the ulnar nerve.
Neurology 30, 873-876 (1980).

JABRE JF.
Surface recording of the H-reflex of the flexor carpi radialis.
Muscle and Nerve 4, 435-438 (1981).

JACKSON L, KEATS AS.
Mechanisms of brachial plexus palsy following anaesthesia.
Anaesthesiology 26, 190-194 (1965).

JAMAL GA, MACLEOD WN.
Electrophysiologic studies in Miller Fisher syndrome.
Neurology 34, 685-688 (1984).

JANKOWSKA E, McCREA D, MACKEL R.
Oligosynaptic excitation of motoneurones by impulses in group Ia muscle spindle afferents in the cat.
Journal of Physiology (London) 316, 411-425 (1981).

JASPER HH, MONNIER AM.
Transmission of excitation between excised non-myelinated nerves. Artificial synapse.
Journal of Cellular and Comparative Physiology 11, 259-277 (1938).

JENNER JR, STEPHENS JA.
Cutaneous reflex responses and their central nervous pathways studied in man.
Journal of Physiology (London) 333, 405-419 (1982).

KADRIE HA, YATES SK, MILNER-BROWN HS, BROWN WF.
Multiple point electrical stimulation of ulnar and median nerves.
Journal of Neurology, Neurosurgery and Psychiatry 39, 973-985 (1976).

KATZ B, SCHMITT OH.
Excitability changes in a nerve fibre during the passage of an impulse in an adjacent fibre.
Journal of Physiology (London) 97, 471-488 (1940).

KERNELL D.
Input resistance, electrical excitability and size of ventral horn cells in cat spinal cord.
Science 152, 1637-1640 (1966).

KIMURA J.
F-wave velocity in the central segment of the median and ulnar nerves. A study in normal subjects and in patients with Charcot-Marie-Tooth disease.
Neurology 24, 539-546 (1974).

KIMURA J.
Collision technique. Physiologic block of nerve impulses in studies of motor nerve conduction velocity.
Neurology 26, 680-682 (1976(a)).

KIMURA J.
A method for estimating the refractory period of motor fibres in the human peripheral nerve.
Journal of the Neurological Sciences 28, 485-490 (1976(b)).

KIMURA J.
F-wave in the evaluation of neurologic disorders. (A comment).
Muscle and Nerve 1, 250-251 (1978(a)).

KIMURA J.
Proximal versus distal slowing of motor nerve conduction velocity in the Guillain-Barre syndrome.
Annals of Neurology 3, 344-350 (1978(b)).

KIMURA J.
The carpal tunnel syndrome. Localisation of conduction abnormalities within the distal segment of the median nerve.
Brain 102, 619-635 (1979).

KIMURA J.
Electrodiagnosis in diseases of nerve and muscle: Principles and Practice.
F.A. Davis. Philadelphia (1983).

KIMURA J, BUTZER JF.
F-wave conduction velocity in Guillain-Barre syndrome. Assessment of nerve segment between axilla and spinal coard.
Archives of Neurology 32, 524-529 (1975).

KIMURA J, BOSCH P, LINDSAY GM.
F-wave conduction velocity in the central segment of the peroneal and tibial nerves.
Archives of Physical Medicine and Rehabilitation 56, 492-497 (1975).

KIMURA J, YAMADA T, RODNITZKY RL.
Refractory period of human motor nerve fibres.
Journal of Neurology, Neurosurgery and Psychiatry 41, 784-790 (1978).

KIMURA J, YAMADA T, STEVLAND NP.
Distal slowing of motor nerve conduction velocity in diabetic poly-neuropathy.
Journal of the Neurological Sciences 42, 291-302 (1979).

KIMURA J, YANAGISAWA H, YAMADA T, MITSUDOME A, SASAHI H, KIMURA A.
Is the F-wave elicited in a select group of motoneurones?
Muscle and Nerve 7, 392-399 (1984).

KING D, ASHBY P.
Conduction velocity in the proximal segments of a motor nerve in the Guillain-Barre syndrome.
Journal of Neurology, Neurosurgery and Psychiatry 39, 538-544 (1976).

KNEZEVIC W, MASTAGLIA FL, THICKBROOM GW, CARROLL WM.
Changes in α-motoneurone excitability during and after voluntary muscle contraction (Abstract).
Electroencephalography and Clinical Neurophysiology 61, S63 (1985).

KORI SH, FOLEY KM, POSNER JB.
Brachial plexus lesions in patients with cancer: 100 cases.
Neurology 31, 45-50 (1981).

KRATZENSTEIN CG.
Schreiben von dem Nutzen der Electricität in der Arzneiwissenschaft.
Halle (1746).

LACHMAN T, SHAHANI BT, YOUNG RR.
Late responses as diagnostic aids in Landry-Guillain-Barre syndrome (Abstract).
Electroencaphalography and Clinical Neurophysiology 43, 147 (1977).

LACHMAN T, SHAHANI BT, YOUNG RR.
Late responses as aids to diagnosis in peripheral neuropathy.
Journal of Neurology, Neurosurgery and Psychiatry 43, 156-162 (1980).

LAMBERT EH, MULDER DW.
Nerve conduction in the Guillain-Barre syndrome (Abstract).
Electroencephalography and Clinical Neurophysiology 17, 86 (1964).

LANCE JW, DE GAIL P, NEILSON PD.
Tonic and phasic spinal cord mechanisms in man.
Journal of Neurology, Neurosurgery and Psychiatry 29, 535-544 (1966).

LANCE JW, NEILSON PD, TASSINARI CA.
Suppression of the H-reflex by peripheral vibration.
Proceedings of the Australian Association of Neurology 5, 45-49 (1968).

LEFEBVRE D'AMOUR M, SHAHANI BT, YOUNG RR, BIRD KT.
The importance of studying sural nerve conduction and late responses in the evaluation of alcoholic subjects.
Neurology 29, 1600-1604 (1979).

LENMAN JAR.
Clinical Neurophysiology.
Blackwell Scientific Publications, Oxford, p.79 (1975).

LLOYD DPC.
Interaction of antidromic and orthodromic volleys in a segmental spinal motor nucleus.
Journal of Neurophysiology 6, 143-151 (1943(a)).

LLOYD DPC.
Conduction and synaptic transmission of reflex response to stretch in spinal cats.
Journal of Neurophysiology 6, 317-326 (1943(b)).

LLOYD DPC.
Post-tetanic potentiation of response in monosynaptic reflex pathways of spinal cord.
Journal of General Physiology 33, 147-170 (1949).

LORENTE de NO R.
Limits of variation of synaptic delay of motoneurones.
Journal of Neurophysiology 1, 187-194 (1938).

LORENTE de NO R.
Transmission of impulses through cranial motor nuclei.
Journal of Neurophysiology 2, 402-464 (1939).

LORENTE de NO R, GRAHAM HT.
Recovery cycle of motoneurones.
American Journal of Physiology 123, 388-399 (1938).

MACCABEE PJ, SHAHANI BT, YOUNG RR.
Usefulness of double simultaneous recording and F-response studies in the diagnosis of carpal tunnel syndrome (Abstract).
Electroencephalography and Clinical Neurophysiology 49, 18P (1980).

McDONAGH MJN, NEWTON JP, YEMM R.
Age changes in motor unit threshold firing rate in the first dorsal interosseous muscle in man (Abstract).
Journal of Physiology (London) 392, 104P (1987).

MACLEOD WN.
Repeater F-waves: A comparison of sensitivity with sensory antidromic wrist-to-palm latency and distal motor latency in the diagnosis of carpal tunnel syndrome.
Neurology 37, 773-778 (1987).

MACLEOD WN, CHERRYMAN G.
M.R.I. and electrophysiological evidence suggesting a secondary functional disturbance of the central nervous system in Fisher's syndrome (Abstract).
Neurology 37(3), Suppl. 1, 366 (1987).

MACLEOD WN, SHAHANI BT.
New electrodiagnostic abnormalities in syringomyelia (Abstract).
Archives of Physical Medicine and Rehabilitation 68, 620 (1987).

McLEOD JG.
H-reflex studies in patients with cerebellar disorders.
Journal of Neurology, Neurosurgery and Psychiatry 32, 21-27 (1969).

McLEOD JG, WRAY SH.
An experimental study of the F-wave in the baboon.
Journal of Neurology, Neurosurgery and Psychiatry 29, 196-200 (1966).

MAGHERINI PD, POMPEIANO O, THODEN U.
The relative significance of presynaptic and postsynaptic effects on monosynaptic extensor reflexes during vibration of synergic muscles.
Archives of Italian Biology 110, 70-89 (1972).

MAGLADERY JW, McDOUGAL DB, Jr.
Electrophysiological studies of nerve and reflex activity in normal man.
1. Identification of certain reflexes in the electromyogram and the conduction velocity of peripheral nerve fibres.
Bulletin of Johns Hopkins Hospital 86, 265-290 (1950).

MAGLADERY JW, PORTER WE, PARK AM, TEASDALL RD.
Electrophysiological studies of nerve and reflex activity in normal man
IV. The two-neurone reflex and identification of certain action potentials from spinal roots and cord.
Bulletin of the Johns Hopskins Hospital 88, 499-519 (1951).

MASTAGLIA FL, CARROLL WM.
The effects of conditioning stimuli on the F-response.
Journal of Neurology, Neurosurgery and Psychiatry 48, 182-184 (1985).

MATTEUCCI C.
Traité des phénomènes electro-physiologiques des animaux, suivi d'études anatomiques sur le système nerveux.
Paris (1844).

MAYER RF, FELDMAN RG.
Observations on the nature of the F-wave in man.
Neurology 17, 147-156 (1967).

MEIENBERG O.
Lesion site in Fisher's syndrome (Letter).
Archives of Neurology 14, 250-251 (1984).

MEYER M.
On the conduction of muscular irritability in paralytic muscles. Hall M.
In: Meyer M. Electricity in Relation to Medical Practice, New York (1872).

MIGLIETTA OE.
The F-response after transverse myelotomy.
In: New Developments in Electromyography and Clinical Neurophysiology.
Ed. Desmedt JE. Vol. 3, pp.323-327, Karger, Basel (1973).

MILLER RG.
The cubital tunnel syndrome: Diagnosis and precise localisation.
Annals of Neurology 6, 56-59 (1979).

MILLS KR.
Orthodromic sensory action potentials from palmar stimulation in the diagnosis of carpal tunnel syndrome.
Journal of Neurology, Neurosurgery and Psychiatry 48, 250-255 (1985).

MISLAWSKY N.
Sur le rôle physiologique des dendrites.
Comptes Rendus des Seances de la Societé de Biologie (Paris) 47, 488-489 (1895).

MORIMOTO K.
Clinical application of the F-wave. II. Frequency of the F-wave.
Kawasaki Medical Journal 6, 49-64 (1980).

MUHLAU G, BOTH R, KUNATH H.
Carpal tunnel syndrome: Course and prognosis.
Journal of Neurology 231, 83-86 (1984).

MÜLLER GJ.
Handbuch der physiologie des menchen.
Coblenz, Holscher, Vol. 1, 856-859 (1835).

NEARY D, OCHOA J, GILLIATT RW.
Sub-clinical entrapment neuropathy in man.
Journal of the Neurological Sciences 24, 283-298 (1975).

NORRIS FH, Jr.
Adult spinal motor neuron disease: Progressive muscular atrophy (Aran's disease) in relation to amyotrophic lateral sclerosis.
In: Vinken PJ, Bruyn CW (Eds), Handbook of Clinical Neurology, Vol. 22 (System Disorders and Atrophies, Part 2. North-Holland Publishing Company, Amsterdam, p.1-56 (1975).

ONGERBOER DE VISSER BW, VAN DER SANDE JJ, KEMP B.
Ulnar F-wave conduction velocity in epidural metastatic root lesions.
Annals of Neurology 11, 142-146 (1982).

ONGERBOER DE VISSER BW, SCHIMSHEIMER RJ, HART AAM.
The H-reflex of the flexor carpi radialis muscle; a study in controls and radiation-induced brachial plexus lesions.
Journal of Neurology, Neurosurgery and Psychiatry 47, 1098-1101 (1984).

PANAYIOTOPOULOS CP.
F-wave conduction velocity in the proximal segment of the tibial nerve.
Muscle and Nerve 1, 181-189 (1978(a)).

PANAYIOTOPOULOS CP.
F-wave conduction velocity in the proximal segment of the deep peroneal nerve: Charcot-Marie-Tooth disease and dytrophia myotonica.
Muscle and Nerve 1, 37-44 (1978(b)).

PANAYIOTOPOULOS CP.
F chronodispersion: a new electrophysiologic method.
Muscle and Nerve 2, 68-72 (1979).

PANAYIOTOPOULOS CP, SCARPALEZOS S.
Chronodispersion of F-wave - A new method to detect abnormal motor nerve function.
Materia Medica Greca 4, 106-108 (1976(a)).

PANAYIOTOPOULOS CP, SCARPALEZOS S.
Muscular dystrophies and motoneurone diseases. A comparative electrophysiologic study.
Neurology 26, 721-725 (1976(b)).

PANAYIOTOPOULOS CP, SCARPALEZOS S.
Dystrophia myotonica: Peripheral nerve involvement and pathogenetic implications.
Journal of the Neurological Sciences 27, 1-16 (1976(c)).

PANAYIOTOPOULOS CP, SCARPALEZOS S.
F-wave studies on the deep peroneal nerve. Part 2. 1. Chronic renal failure. 2. Limb-girdle muscular dystrophy.
Journal of the Neurological Sciences 31, 331-334 (1977).

PANAYIOTOPOULOS CP, SCARPALEZOS S, NASTAS PE.
F-wave studies on the deep peroneal nerve. Part 1. Control subjects.
Journal of the Neurological Sciences 31, 319-329 (1977).

PANAYIOTOPOULOS CP, LAGOS G.
Tibial nerve H-reflex and F-wave studies in patients with uraemic neuropathy.
Muscle and Nerve 3, 423-426 (1980).

PEIOGLOU-HARMOUSSI S, HOWEL D, FAWCETT PRW, BARWICK DD.
F-response behaviour in a control population.
Journal of Neurology, Neurosurgery and Psychiatry 48, 1152-1158 (1985(a).

PEIOGLOU-HARMOUSSI S, FAWCETT PRW, HOWEL D, BARWICK DD.
F-responses: A study of frequency, shape and amplitude characteristics in healthy control subjects.
Journal of Neurology, Neurosurgery and Psychiatry 48, 1159-1164 (1985(b)).

PEIOGLOU-HARMOUSSI S, FAWCETT PRW, HOWEL D, BARWICK DD.
F-responses in syringomyelia.
Journal of the Neurological Sciences 75, 293-304 (1986).

PEIOGLOU-HARMOUSSI S, FAWCETT PRW, HOWEL D, BARWICK DD.
F-response frequency in motor neurone disease and cervical spondylosis.
Journal of Neurology, Neurosurgery and Psychiatry 50, 593-599 (1987(a)).

PEIOGLOU-HARMOUSSI S, DIMITRIADIS A, ANTONIOU S, NOITSI-MICHALI F, LOGOTHETIS J.
F-waves in evaluating uraemic polyneuropathy: a long-term study after the application of continuous ambulatory peritoneal dialysis.
Functional Neurology 2, 195-205 (1987(b)).

PERFETTI CC, LORIZIO A.
Sulla presenza di riposte assoniche in soggetti affetti da sla.
Rivista di Neurobiologia 13, 937-942 (1967).

PETAJAN JH.
F-waves in neurogenic atrophy.
Muscle and Nerve 8, 690-696 (1985).

PHALEN GS.
Spontaneous compression of the median nerve at the wrist.
Journal of the American Medical Association 145, 1128-1133 (1951).

PHALEN GS.
Reflections on 21 years' experience with carpal tunnel syndrome.
Journal of the American Medical Association 212, 1365-1367 (1970).

PHILLIPS MS, STEWART S, ANDERSON JR.
Neuropathological findings in Miller Fisher syndrome.
Journal of Neurology, Neurosurgery and Psychiatry 47, 492-495 (1984).

PINELLI P, VALLE M.
Studio fisiopatologica dei reflessi muscolari nelle paresi spastiche (sui tests per la misura della spasticita).
Archivo per le Scienze Mediche (Torino) 110, 77-203 (1960).

PIPER H.
Über die leitungsgeschwindigkeit in den markhaltingen, menschlichen neren.
Pflügers Archiv für die Gesamte Physiologie des Menschen und Der Tiere (Bonn).
124, 591-600 (1908).

PIPER H.
Elektrophysiologie Menschlicher Muskeln.
Berlin (1912(a)).

PIPER H.
Die aktionsströme menschlicher muskeln. Die methodik der untersuchung am saitengalvanometer und die prinzipien der stromkurvenanalyse. Typenunterschiede der willkürkontraktion.
Zeitschrift für Biologische Technik und Methodik (Strassburg) 3, 52-68 (1912(b)).

RENSHAW B.
Influence of discharge of motoneurons upon excitation of neighbouring motoneurons.
Journal of Neurophysiology 4, 167-183 (1941).

RICHTER R.
The ataxic form of polyradiculoneuritis (Landry-Guillain-Barré syndrome): Clinical and pathologic observations.
Journal of Neuropathology and Experimental Neurology 21, 171-184 (1962).

ROPPER AH.
The C.N.S. in Guillain-Barre syndrome (Editorial).
Archives of Neurology 40, 397-398 (1983).

ROPPER AH, SHAHANI BT.
Proposed mechanism of ataxia in Fisher's syndrome (Abstract).
Archives of Neurology 40, 537-538 (1983).

ROSSIER AB, FOO D, SHILLITO J, DYRO FM.
Post-traumatic cervical syringomyelia.
Brain 108, 439-461 (1985).

ROTH G.
Vitesse de conduction motrice du nerf median dans le canal carpien.
Annales de Medecine Physique 13, 117-132 (1970).

ROTH G.
Intranervous regeneration. The study of motor axon reflexes.
Journal of the Neurological Sciences 41, 139-148 (1979).

ROTH G.
Fasciculations and their F-response. Localisation of their axonal origin.
Journal of the Neurological Sciences 63, 299-306 (1984).

SAWHNEY BB, KAYAN A.
A study of axon reflexes in some neurogenic disorders.
Electromyography 3, 297-305 (1970).

SAWHNEY BB, KAYAN A.
A study of the F wave from the facial muscles (Abstract).
Electroencephalography and Clinical Neurophysiology 30, 261 (1971).

SCHEIPPATI M.
The Hoffmann reflex: A means of assessing spinal reflex excitability and its descending control in man.
Progress in Neurobiology 28, 345-376 (1987).

SCHILLER HH, STÅLBERG E.
F responses studied with single fibre EMG in normal subjects and spastic patients.
Journal of Neurology, Neurosurgery and Psychiatry 41, 45-53 (1978).

SCHIMSHEIMER RJ, ONGERBOER DE VISSER BW, KEMP B.
The flexor carpi radialis H-reflex in lesions of the sixth and seventh cervical nerve roots.
Journal of Neurology, Neurosurgery and Psychiatry 48, 445-449 (1985).

SHAHANI BT, YOUNG RR.
Effect of vibration on the F response.
In: Motor System: Neurophysiology and Muscle Mechanisms. Ed. Shahani M. Elsevier, Amsterdam. pp.189-195 (1976).

SHAHANI BT, SUMNER AJ.
Electrophysiological studies in peripheral neuropathy: early detection and monitoring.
In: Clinical Neurophysiology, Ed: Stålberg E, Young RR, Butterworth's, London, Chapter 6, p.133 (1981).

SHAHANI BT, POTTS F, DOMINGUE J.
F response studies in peripheral neuropathies (Abstract).
Neurology 30, 409-410 (1980(a)).

SHAHANI BT, POTTS F, JUGUILON A, YOUNG RR.
Maximal-minimal motor nerve conduction and F response studies in normal subjects and patients with ulnar compression neuropathies (Abstract).
Muscle and Nerve 3, 182 (1980(b)).

SHAHANI BT, POTTS F, JUGUILON A, YOUNG RR.
Electrophysiological studies in "thoracic outlet syndrome".
Muscle and Nerve 3, 182-183 (1980(c)).

SHAHANI BT, MACLEOD WN, BERTICS G.
Minimal F response latencies as a measure of conduction in largest-diameter alpha motor axons (Abstract).
Neurology (Suppl. 1). 37, 114 (1987).

SHAWE GDH.
On the numbers of branches formed by regenerating nerve fibres.
British Journal of Surgery 42, 474-488 (1955).

SIMPSON JA.
Electrical signs in the diagnosis of carpal tunnel and related syndromes.
Journal of Neurology, Neurosurgery and Psychiatry 19, 275-280 (1956).

STÅLBERG E, TRONTELJ JV.
Demonstration of axon reflexes in human motor nerve fibres.
Journal of Neurology, Neurosurgery and Psychiatry 33, 571-579 (1970).

STÅLBERG E, TRONTELJ JV, TRONTELJ M.
The jitter of single human muscle fibre responses to stimulation of the motor axon (Abstract).
Electroencephalography and Clinical Neurophysiology 34, 818 (1973).

STÅLBERG E, THIELE B.
Motor unit fibre density in the extensor digitorum communis muscle. Single fibre electromyographic study in normal subjects at different ages.
Journal of Neurology, Neurosurgery and Psychiatry 38, 874-880 (1975).

STANLEY EF.
Reflexes evoked in human thenar muscles during voluntary activity and their conduction pathways.
Journal of Neurology, Neurosurgery and Psychiatry 41, 1016-1023 (1978).

SUNDERLAND S.
Nerves and Nerve Injuries.
Williams and Wilkins, Baltimore, pp.140-142 (1968).

SWAMMERDAM J.
Biblia Naturae.
(Translation into English from the Dutch and Latin original edition by T. Flloyd). The Book of Nature. With the life of the author by H. Boerhaave. Revised by J. Hill, London (1758).

TEASDALL RD, PARK AM, LANGUTH HW, MAGLADERY JW.
Electrophysiological studies of reflex activity in patients with lesions of the nervous system. II. Disclosure of normally suppressed monosynaptic reflex discharge of spinal motoneurones by lesions of lower brain-stem and spinal cord.
Bulletin of the Johns Hopkins Hospital 91, 245-256 (1952).

THOMAS JE, LAMBERT EH.
Ulnar nerve conduction velocity and H reflex in infants and children.
Journal of Applied Physiology 15, 1-9 (1960).

THORNE J.
Central responses to electrical activation of the peripheral nerves supplying the intrinsic hand muscles.
Journal of Neurology, Neurosurgery and Psychiatry 28, 482-495 (1965).

TONZOLA R, ACKIL A, SHAHANI BT, YOUNG RR.
Usefulness of electrophysiological studies in the diagnosis of lumbosacral root disease (Abstract).
Electroencephalography and Clinical Neurophysiology 49, 17 (1980).

TRONTELJ JV.
A study of the H-reflex by single fibre EMG.
Journal of Neurology, Neurosurgery and Psychiatry 36, 951-959 (1973).

TRONTELJ JV, TRONTELJ M.
F-responses of human facial muscles. A single motoneurone study.
Journal of the Neurological Sciences 20, 211-222 (1973).

UPTON ARM, McCOMAS AJ.
The double crush in nerve-entrapment syndromes.
Lancet 2, 359-361 (1973).

UPTON ARM, McCOMAS AJ, SICA REP.
Potentiation of 'late' responses evoked in muscles during effort.
Journal of Neurology, Neurosurgery and Psychiatry 34, 699-711 (1971).

VEALE JL, REES S.
Renshaw cell activity in man.
Journal of Neurology, Neurosurgery and Psychiatry 36, 674-683 (1973).

WALL PD, JOHNSON AR.
Changes associated with post-tetanic potentiation of a monosynaptic reflex.
Journal of Neurophysiology 21, 148-158 (1958).

WEAVER RA, LANDAU WM, HIGGINS JF.
Fusimotor function. Part II. Evidence of fusimotor depression in human spinal shock.
Archives of Neurology (Chicago) 9, 127-132 (1963).

WEBER RJ, PIERO DL.
F wave evaluation of thoracic outlet syndrome: A multiple regression derived F wave latency predicting technique.
Archives of Physical Medicine and Rehabilitation 59, 464-469 (1978).

WILLER JC.
Étude de la vitesse de conduction des fibres sensitives Ia chez l'homme normal par la méthode du réflex "H".
Electroencephalography and Clinical Neurophysiology 38, 329-330 (1975).

WOHLFART G.
Regenerative phenomena in the muscle nerves in connection with poliomyelitis and amyotrophic lateral sclerosis.
Nordisk Medicia (Stockholm) 54, 1075-1078 (1955).

WULFF CH, GILLIATT RW.
F waves in patients with hand wasting caused by a cervical rib and band.
Muscle and Nerve 2, 452-457 (1979).

YATES SK, BROWN WF.
Characteristics of the F-response: A single motor unit study.
Journal of Neurology, Neurosurgery and Psychiatry 42, 161-170 (1979).

YEMM R.
The representation of motor-unit action-potentials on the skin-surface electromyograms of the masseter and temporal muscles in man.
Archives of Oral Biology 22, 201-205 (1977).

YOUNG RR, SHAHANI BT.
Clinical value and limitations of F-wave determination (Letter).
Muscle and Nerve 1, 248-250 (1978).

APPENDIX

[*From the Proceedings of the Physiological Society*, 23–24 *June* 1986
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Variations in neuronal response to antidromic invasion (F-response) of spinal α motor neurone pools subserving abductor pollicis brevis (A.P.B.), abductor digiti minimi (A.D.M.) and extensor digitorum brevis (E.D.B.) in man

By W. N. Macleod (introduced by G. C. Leslie). *Section of Neurology, Department of Medicine, Ninewells Hospital and Medical School, Dundee University, Dundee DD1 9SY*

Antidromic invasion of the anterior horn cell pool of a mixed peripheral nerve generates recurrent activity in only a minute fraction of α neurones (α MN) (Magladery & McDougal, 1950). During prolonged periods of stimulation of the ulnar nerve each neurone discharges an F-response only infrequently, if at all, and its activity varies with time (Schiller & Stålberg, 1978). The physiological mechanisms which determine these patterns of restricted and variable backfiring are incompletely understood, but it is known that the F-generating capacity of an α MN in the human median nerve is not directly related to its peripheral excitability and impulse-conducting properties (Kimura *et al.* 1984).

I have studied F-wave production in three different α MN pools: two in the lower cervical/upper thoracic spine and one in the caudal spine of healthy volunteers who gave their informed consent. The study had ethical approval.

A total of 231 ulnar (to A.D.M), 223 median (to A.P.B.) and 103 deep peroneal (to E.D.B.) nerves to over 100 subjects were stimulated with supramaximal shocks (20 % supramaximal for the M-response) at either wrist or ankle; 100 stimuli were applied to each nerve at 1 Hz and F-wave sweeps were recorded on photographic paper from the electromyograph on a raster setting.

Two measurements were made: (1) the N.F.R. value – the number of stimuli/nerve which evoked no F-response ($< 40\ \mu V$); (2) the % RF-wave value – percentage value of recurring identical F-wave-forms/number of F-waves ($\geqslant 40\ \mu V$) recorded.

The statistics (mean $\pm$ S.D.) for the N.F.R. values for ulnar, median and peroneal nerves were $8{\cdot}7 \pm 13{\cdot}0$, $17{\cdot}1 \pm 16{\cdot}1$, $52{\cdot}9 \pm 25{\cdot}8$ and for the % RF-wave values they were respectively $8{\cdot}9 \pm 7{\cdot}2$, $14{\cdot}8 \pm 12{\cdot}2$, $53{\cdot}6 \pm 21{\cdot}6$. The differences between each of the three neurone pools were highly significant ($P \ll 0{\cdot}001$) for both N.F.R. and % RF-wave values, and indicate that these F-generator pools behave very differently in response to antidromic invasion. The most striking difference was between the upper and lower limb nerves. The peroneal α MN bodies are less responsive, with a higher proportion of cells inactive as F-generators, while a very restricted sub-population have membrane characteristics which favour F-wave production.

Modification of the control of F-wave production results from a variety of disorders of peripheral nerve (Macleod, 1986). The differences in the F-generators at different sites in the spinal cord must be appreciated before the modifying effects of pathological neurological disorders can be evaluated.

REFERENCES

Kimura, J. *et al.* (1984). *Muscle & Nerve* **7**, 392–399.
Macleod, W. N. (1986). (submitted for publication).
Magladery, J. W. & McDougal, D. B. (1950). *Bull. Johns Hopkins Hosp.* **86**, 265–290.
Schiller, H. H. & Stålberg, E. (1978). *J. Neurol. Neurosurg. Psychiat.* **41**, 45–53.

rticle abstract—Thirty-five thousand six hundred supramaximal shocks were applied to 209 healthy and 147 entrapped edian nerves (carpal tunnel syndrome—CTS) to characterize the backfiring behavior of the alpha motor neuron pool of ɔductor pollicis brevis in health and the modifying effect of a compressive neuropathy. A contraction of the normal subpopula-ɔn of active F-wave generators was found in CTS, while active neurons backfired at higher than normal frequencies ($p < 0.001$). hese modifications in spinal behavior are reflected in the % Repeater F-wave value, whose sensitivity in the detection of CTS ɔproaches that of sensory wrist-to-palm latency estimation. This technique offers an alternative to latency measurement in the agnosis of CTS. An economical strategy for the electrodiagnosis of CTS is proposed.

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Repeater F waves:

A comparison of sensitivity with sensory antidromic wrist-to-palm latency and distal motor latency in the diagnosis of carpal tunnel syndrome

William N. Macleod, MBChB, MRCP

ugelberg's demonstration[1] of a decline in motor fiber ɔnduction velocity across an experimentally com-ɛssed nerve segment was the forerunner of elec-odiagnostic tests which are currently used to detect ıtrapment neuropathies. When a median nerve is ɔmpressed within the carpal tunnel, optimal elec-odiagnostic return is obtained from selective scrutiny the damaged wrist-to-palm segment, as electro-ıysiologic abnormalities are often confined to that ngth of the nerve.[2-6]

There are numerous methods available for the study the wrist-to-palm portion of the median nerve, using ther sensory or motor fibers, or both.[7-9] Kimura[6] was ɔle to localize focal dysfunction under the transverse rpal ligament using an "inching" technique. Such chniques, and variations on them, currently represent e most sensitive and most widely used means of con-ɛming the clinical impression of carpal tunnel syn-ome (CTS).[10]

An alternative approach to defining nerve compres-ɔn entails analysis of F-response latencies. In CTS, ey can be prolonged, and if the latency difference oduced by median stimulation proximal and distal to e carpal tunnel is calculated, sensitivity can be in-eased.[11-13] Eisen et al[12] have applied F-wave latency easurements to the differentiation of proximal and stal upper limb entrapments and found that signifi-nt numbers of patients diagnosed as having CTS have existing proximal lesions.

The use of ulnar/median latency or amplitude ratios ıs been suggested, but is unsatisfactory as it assumes rfect ulnar function.[14]

In the electrodiagnostic confirmation of CTS, all esently used methods measure impaired nerve con-ıction velocity. This is done by measuring latencies across nerve segments and by observing reductions in the sensory action potential (SAP) or compound muscle action potential amplitude, as such reductions reflect conduction block or focally slowed conduction with temporal dispersion.

This paper describes a method of identifying median nerve malfunction (secondary to entrapment), which is not primarily a measurement of latency (conduction velocity). Instead, the backfiring frequencies of the neurons in the F-wave generator pool subserving abductor pollicis brevis (APB) are quantified.

Renshaw,[15] experimenting on anesthetized cats, detected late-onset, low-voltage deflections over ventral rootlets in which he had set up an antidromic volley. Magladery and McDougal[16] later named these potentials F waves in man and commented on their variability with consecutive stimuli. The experiments of Schiller and Stålberg[17] on healthy human axons indicate a differential F-generating capacity for the alpha axons within an individual mixed nerve. The majority of healthy motor neurons fail to discharge an F wave when stimulated repeatedly with supramaximal shocks, and those which do are active only intermittently and infrequently. Factors which modify anterior horn cell (AHC) membrane characteristics might be expected to alter their backfiring patterns. This paper reports an analysis of the backfiring characteristics of the alpha motor neuron (α MN) pool subserving APB in a group of 209 control subjects and in a group of 147 cases of CTS confirmed by Kimura's sensory (antidromic) wrist-to-palm latency (SAWPL) technique.[6]

Materials and methods. *Subjects.* Group I. One hundred twenty-five healthy subjects, 60 males and 65 females, aged 17 to 82 (mean 41), were included to

ɪm the University Department of Medicine, Ninewells Hospital and Medical School, and the Section of Neurology, Royal Infirmary, Dundee, Scotland, UK.

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ıress correspondence and reprint requests to Dr. Macleod, E.M.G. Lab, Massachusetts General Hospital, Boston, MA 02144.

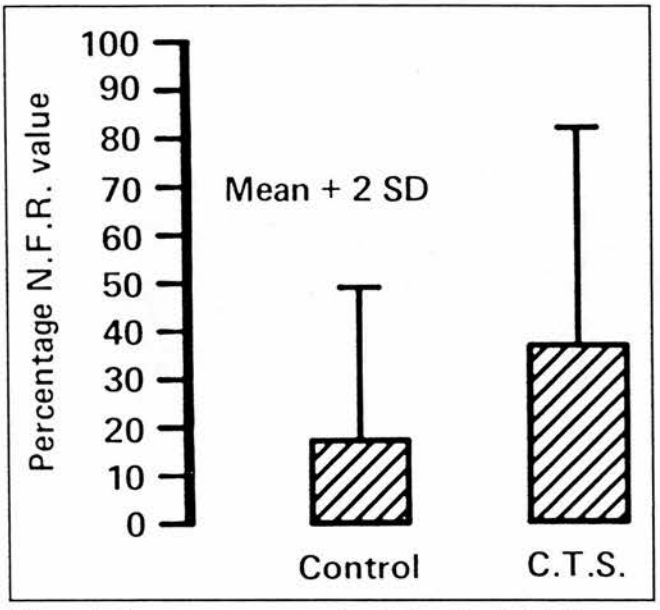

Figure 1. Percent of supramaximal stimuli which failed to elicit an F wave of >40 μV: no F wave response (NFR) value of control group and carpal tunnel syndrome (CTS) group.

establish control values for median nerve F-wave parameters (see "Methods," below). Each subject was free of symptoms of nervous system dysfunction, had no known medical condition which predisposed to neuropathy, was not exposed to known neurotoxic drugs, had no neurologic signs, and had no family history of a genetically linked neurologic disorder. Volunteers came from hospital staff and included doctors, medical students, nurses, porters, cleaners, and laboratory technicians. Volunteers also came from the neurology clinic when their diagnosis was of vascular or tension headache. Two hundred nine "healthy" median nerves were evaluated.

Group II. From group I, 26 subjects (15 female and 11 male, aged 17 to 63, with a mean age of 39) were evaluated to establish normal values for SAWPLs. Fifty-two (healthy) median nerves were studied.

Group III. One hundred eleven consecutive patients with symptomatic CTS confirmed by an abnormal SAWPL (≥1.8 msec) had, on the same visit to the EMG Laboratory, an evaluation of F responses through the median nerve and measurement made of the distal motor latency (DML). These patients were referred for elecrodiagnostic tests from the Neurology Clinic, the Orthopaedic/Hand Clinics, and rarely, General Surgery and General Medical Clinics or wards. None of the CTS subjects had reflex changes or objective signs of any additional neurologic disorder. One hundred forty-seven symptomatic median nerves were evaluated.

Methods 1. The neurophysiologic assessments were standardized. They were done with the patient lying comfortably in an ambient temperature maintained above 26 °C. If the patient's forearm volar skin temperature was less than 34 °C, the patient was warmed, using hot water bottles and blankets to >34 °C.

Sensory antidromic wrist-to-palm latency. An 8-cm length of median nerve was examined in the manner described by Kimura.[6] The distal skin crease of the wrist was taken to lie over the proximal edge of the transverse carpal ligament. Stimuli were applied at three sites proximal and five sites distal to this point over the course of the median nerve, with 1 cm between each stimulus site. Stimuli were delivered through a saddle-type bipolar electrode, with the anode sited 2 cm proximal to the cathode. The intensity and duration of the shock was adjusted to maximize the SAP. Recording of the antidromic SAP was made using saline-soaked, lint-covered silver strips formed as ring electrodes over the proximal and distal interphalangeal joints of the index finger. Latencies were measured at SAP peaks on either a Medelec MS8 or MS6 EMG.

F-response recording. Initially, each median nerve was stimulated at the wrist to produce a maximal M response (duration: 50 μsec for control subjects, 50 to 200 μsec for CTS patients). The cathodal position was then reversed to a proximal placement, and 100 stimuli, 20% supramaximal, were delivered at 1 Hz. The recording electrode was located over the belly of APB, and the reference electrode was just distal to the metacarpophalangeal joint.

Using either a Medelec MS6 or MS8 EMG on a Raster recording setting, 100 F-wave sweeps were photographed for subsequent analysis. Each vertical division represented 200 μV, and the sweep speed was 5 msec/cm on the Medelec MS6 and 6.25 msec/cm on the Medelec MS8. Subjects were tested supine and encouraged to relax, to minimize possible facilitating effects on F-wave formation by muscle contraction.[18]

The 100 sweeps from each nerve were analyzed, and two measurements were made: (1) The number of recurring identical F waves generated by each nerve was calculated. To be regarded as identical, each F wave was required to have the same latency, configuration, and amplitude. These recurring identical F waves were termed Repeater F waves (RF-waves). Only F waves with a peak-to-peak amplitude ≥40 μV were included in the measurement. Responses of lower amplitude proved impossible to analyze with any degree of reliability. Very minor movements, eg, twitch induced by the stimulus, could make considerable changes to the size and shape of these potentials.[2] The number of sweeps per nerve where the response was <40 μV was calculated. These sweeps are designated as no F-wave response (NFR).

Methods 2. All subjects diagnosed as having CTS had a thorough clinical neurologic examination. Phalen's and Tinel's tests were done on each. A careful history of each patient's symptoms was obtained to identify the characteristics of the presentation.

Results. The NFR value for the CTS group was significantly higher ($p < 0.001$) than for the control group: mean (+ SD), 36.8 (22.6) and 17.3 (16.1), respectively (figure 1). Both groups had in common a very wide range (control, 0 to 75; CTS, 0 to 97). NFR, taken as an isolated parameter, is therefore an insensitive index of nerve compression in the vast majority of cases. The

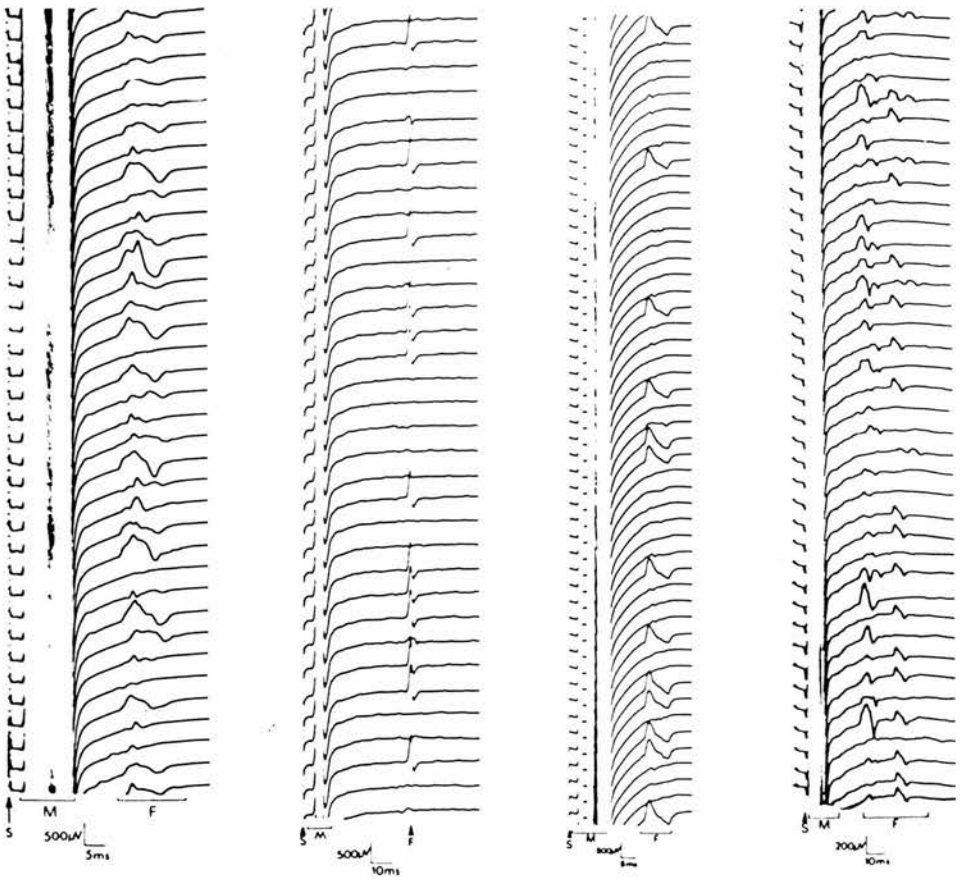

Figure 2. Trace 1: F-wave sweeps from a healthy median nerve. Two F-waves recur; %Repeater F-wave (%RF) value = 12%. Trace 2: F-wave sweeps from a CTS. A high-frequency Repeater F-wave (RF) follows the majority of supramaximal stimuli at a delayed latency. Trace 3: F responses from a CTS nerve with a high %RF value; two high-frequency RF waves predominate. Trace 4: RF waves firing "in series" (CTS). Two individual RF waves follow the initial F responses at a high frequency.

number of RF-waves obtained from an individual CTS nerve also had a broad range (3 to 100), and characteristically, when there was a low RF-wave count there was a high NFR value. When a damaged nerve backfired frequently (eg, 95 F waves per 100 stimuli), there was a high RF-wave count (eg, 75/95 responses). It therefore appears that there are two factors at work within the F-generator pool consequent upon the peripheral nerve lesion: (1) a reduction from normal in the size of the α MN subpopulation liable to generate an F response, and (2) an enhanced backfiring capacity in a select fraction of the AHC population. Although the CTS group contained an increased number of RF-waves compared with the control group ($p < 0.001$), the presence of a low F-response frequency in many cases meant that the RF-wave counts in damaged nerves could be within the range seen in the control group. To take account of the contracted backfiring population, the RF-wave count was calculated as a percentage of the F responses obtained (≥ 40 μV), rather than as percentage of M responses obtained. This value is termed %Repeater F-wave value (%RF value). Figure 2, first trace, shows F-wave sweeps from a control median nerve. This nerve displays a high F-wave response frequency with four RF-waves. The %RF value is 12%. Figure 2, second trace, shows F-wave sweeps from a CTS patient. A single delayed-latency RF-wave recurs (in 100 F sweeps, the NFR value was 92, no other RF-wave forms were obtained, and the total %RF value was 82%). The third trace in figure 2 shows median nerve responses from another CTS patient where there are two normal-latency, high-frequency RF-waves comprising a high %RF value. Another feature which may be seen in damaged nerves is that of repeater waves appearing "in series." The final trace, figure 2, shows F waves appearing in series. The initial F waves do not have an abnormal %RF value, but a high-frequency Repeater F-wave occurs in 16 of the 39 sweeps pictured. In five of the sweeps, there is an even longer-latency RF-wave. No formal analysis was made of serial F responses in the control group. However, serial responses were rare, and Repeater waves in series were not observed. The analysis of RF-waves in this study does not take into account serial Repeaters; only the initial F response was included in the analysis. In the CTS group, many of the Repeater waves which were identified occurred within the normal latency range for median nerve F responses. There was a significant rise in the %RF value from the control to the CTS group of 14.9 $\pm$ 12.2 to 59.1 $\pm$ 23.5 (mean $\pm$ SD) ($p < 0.001$). Figure 3 displays %RF values of the subjects from both groups. As the %RF values did not form a normal distribution, a reference range for the control group was determined using a cumulative frequency curve. Figure 4 shows the 90% and 95% upper

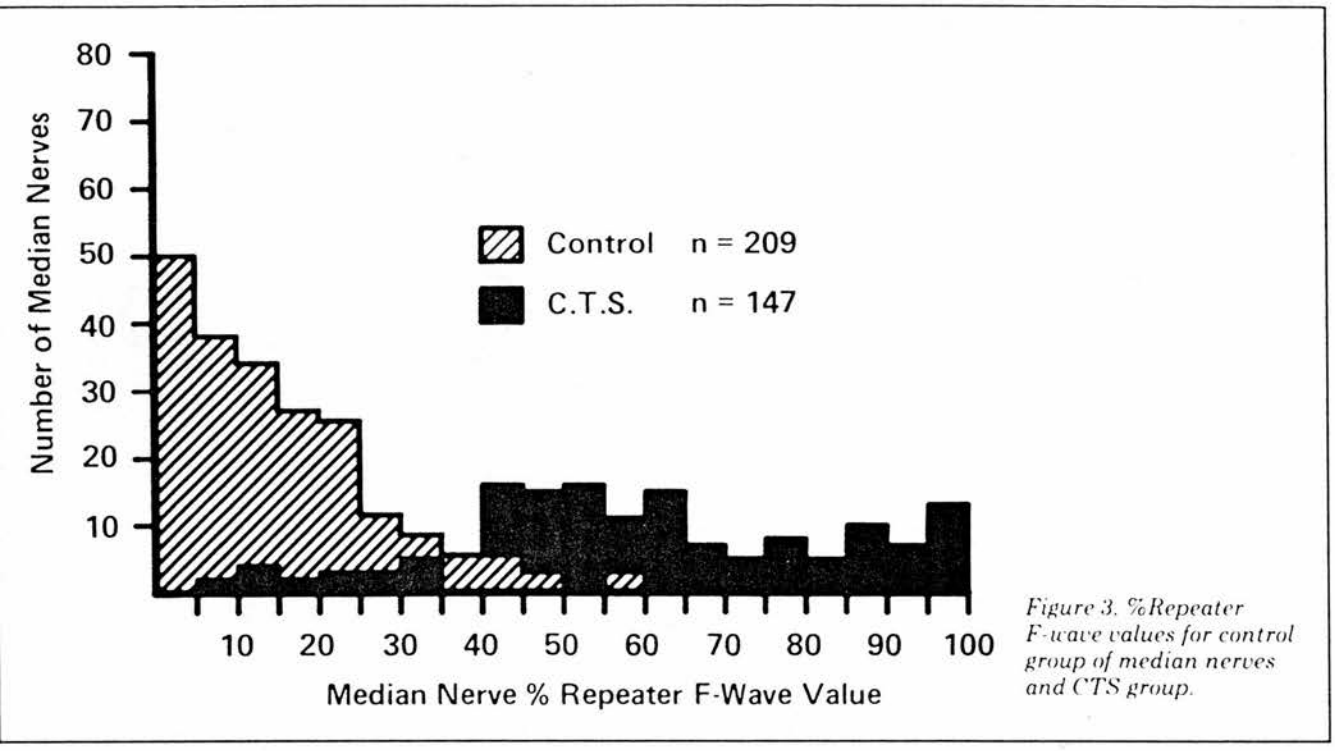

Figure 3. %Repeater F-wave values for control group of median nerves and CTS group.

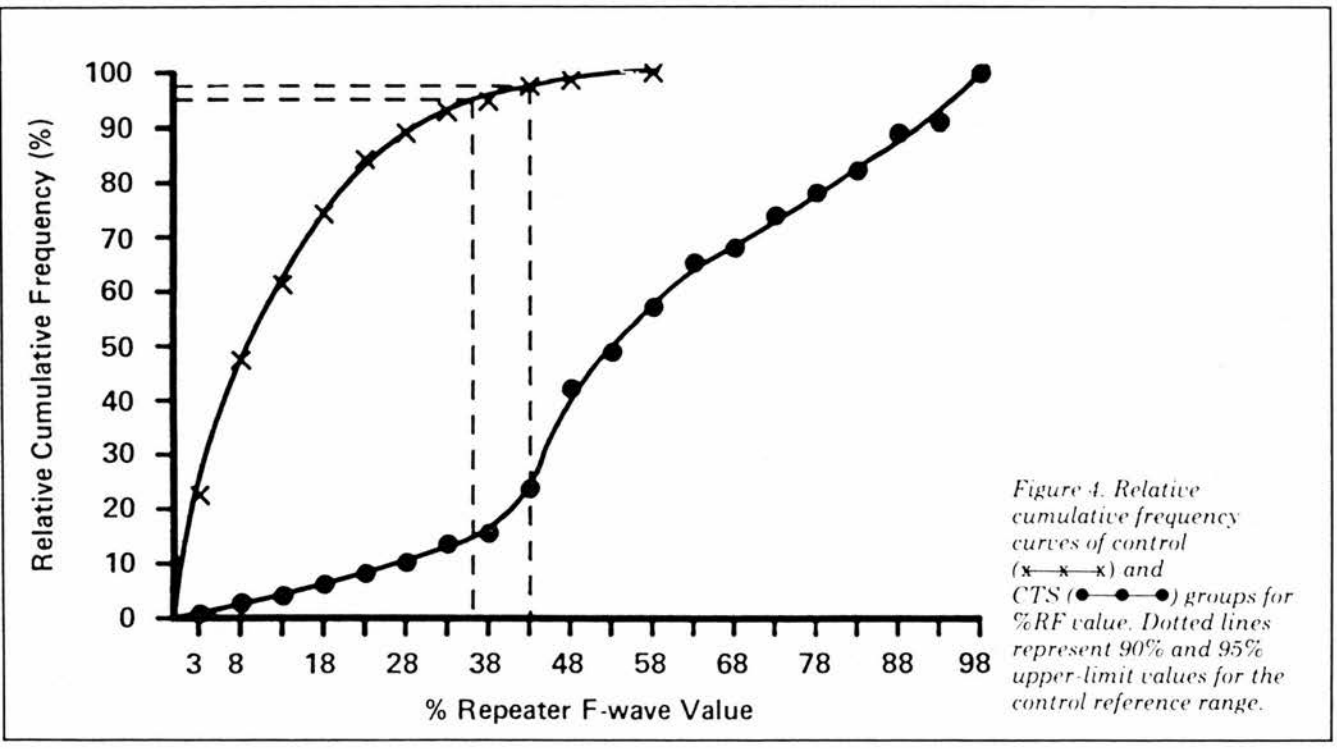

Figure 4. Relative cumulative frequency curves of control (×—×—×) and CTS (●—●—●) groups for %RF value. Dotted lines represent 90% and 95% upper-limit values for the control reference range.

limits of the reference range at 36.5% and 43%, respectively; 84.4% of CTS %RF values lay outside the control reference range 90% upper limit.

The range of latencies for the SAWPL in the control group was 1.1 to 1.7 msec. The mean latency was 1.49 msec (SD, 0.157).

Phalen's test was positive in 32% of cases and Tinel's test positive in only 21% of cases.

Distal motor latency was <4.5 msec in 65.4% of CTS cases and >4.8 msec in 28.5% of cases.[19,22,27]

Discussion. When Phalen[20] reported 11 cases of CTS to the American Medical Association in 1950, the diagnosis was a novel one. It is now the most commonly

ncountered peripheral nerve entrapment syndrome.[21] lectrodiagnosis took some time to catch up with and ubsequently overtake the clinical definition of the syn-rome.[6,12,22,27] In 1970, Phalen,[23] with an extensive clini-al experience of the condition, wrote that "CTS may be resent with no evidence of electromyographic abnor-nalities." It is clear from this series of 147 median ntrapments that the key clinical features (such as umb waking, objective/subjective sensory disturbance ocalized to median territory, or relief from wrist flick-ng) which may alert the clinician to a median en-rapment are frequently absent.[24-26] Many patients in his series had nonspecific, ill-defined sensory distur-ance and discomfort extending beyond or even not nvolving the median territory. Phalen found that the rist flexion test and Tinel's sign were present in ap-roximately 70% of his cases, but in this series, the gure was nearer 30% for the former and 20% for the tter, reflecting the use of increasingly sophisticated erve conduction studies to confirm atypical presenta-ons of median nerve entrapment. Phalen's test ap-ears to be of most use in suggesting the diagnosis of nedian compromise when the symptoms are atypical, ut can be reproduced perfectly by forced flexion of the rist (one patient, interestingly, obtained relief from ontinuous symptoms by forced flexion for 30 seconds). dditional difficulties in clinical diagnosis are not un-ommon; the coexistence of a neurologic disorder (such s cervical spondylotic radiculopathy, multiple scle-osis, or diabetic neuropathy) or a rheumatic condition such as severe rheumatoid arthritis) may produce signs nd symptoms in the median territory which mask oncomitant but nonetheless significant CTS. If a cor-ect diagnosis of CTS is not reached early, several un-ortunate consequences may ensue. For example, relevant spondylotic change on a neck x-ray may lead o the mistaken attribution of symptoms to degener-tive spondylosis, and to the use of analgesics, a cervical ollar, neck traction, or even cervical surgery.

For these reasons (ie, atypical and masked presenta-ons), it is clear that a sensitive test for CTS is re-uired, and particularly so if surgery is contemplated, hen a confident diagnosis is essential. Progression to enar wasting and weakness implies a retarded diagno-s and therapeutic intervention. The aim must be to dentify the lesion in advance of a potentially irrevers-le deterioration in sensory and motor function, as the resence of a severe lesion tends to be associated with a oorer response to surgical decompression.[28]

Kimura's SAWPL technique[6] is sensitive and simple o perform. For these reasons, it was used as a yardstick o assess the sensitivity of the %RF value in identifying TS. It is clear that significant numbers of patients ith atypical presentations of CTS cannot be clinically iagnosed, and some are likely to escape identification y the nerve conduction studies currently in use. As RF-ave analysis quantifies an additional and distinct as-ect of neural dysfunction, it is tempting to hope that dditional cases might be detected through its use. The %RF value was increased above the 90% reference ange in 84.4% of CTS cases, while the DML values ere falsely negative in 65% of cases. The %RF value is a more sensitive index of entrapment than is the DML and approaches the sensitivity of the SAWPL.

One patient was encountered outside this study who had symptoms compatible with CTS, but whose SAWPL was clearly normal (1.4 msec), with a %RF value of 80%, and who had a prolonged DML of 5.2 msec. This demonstrates that sensory fibers can be selectively spared when motor function is compromised and that the %RF value can indicate an entrapment while the SAWPL remains normal. It also highlights the importance of performing DML (or transtunnel motor fiber evaluation), even though DML is falsely negative in a high percentage of cases. A small number of patients with classical CTS symptoms and signs (sensory splitting of the fourth finger) who have had borderline SAWPL values have been seen to display grossly abnormal %RF values (outside the 95% reference range), suggesting that the %RF value may detect lesions which SAWPL does not. Another patient with nonspecific brachalgia and ill-localized hand paresthesias without objective signs had no abnormality of conventional nerve conduction studies, but had a %RF value of 73%. No active therapy was ordered, and 3 months later, the patient's symptoms worsened; on repeat evaluation, the SAWPL had become abnormal at 2.2 msec (previously 1.6 msec). It therefore appears likely that the %RF value may prove useful in detecting lesions which are not associated with focal slowing of sensory conduction under the transverse carpal ligament. This contention requires evaluation of a large group of patients, pre- and postsurgery, and is currently in progress.

Identification of RF-waves is usually easy, especially when there is a high NFR value. Axon reflexes and H reflexes, by their nature, are not likely to be a source of confusion, as both disappear with high intensity shocks.[29]

Single-fiber EMG studies show that the F response through a single alpha neuron has a jitter of less than 70 μsec (usually <30 μsec), supporting Dawson and Merton's concept of the F wave originating from a backfiring AHC.[17,30] In his original observations, Renshaw[15] noted that only a limited number of alpha neurons discharged a backfired response on receipt of an afferent volley. Schiller and Stålberg[17] have since studied the F-response frequency of healthy individual motor neurons and found that the majority failed to backfire. Those that did, backfired infrequently and in bursts. Backfiring from an individual α MN with consecutive stimuli was very rare. The mechanism whereby a peripheral nerve compression further contracts the backfiring alpha neuron pool and facilitates backfiring at an increased frequency in some cells in that subpopulation is obscure. A failure to activate axons (in part related to conduction block) and modification of AHC membrane potentials through altered sensory input are likely elements. APB spindle sensitivity can be modified by damage to gamma efferent fibers, and the input through group IA and II fibers may be further modified by compressive damage. There may be a disequilibration of spindle input, allowing relatively more antagonistic reciprocal inhibition of the majority of neurons under test.

Identical changes in AHC backfiring behavior result from a variety of neuropathologic processes affecting the peripheral nervous system, eg, acute demyelination of cervical roots (as in the Guillain-Barré syndrome) and primary disorders of the α MN (as in spinal muscular atrophy). Care is therefore necessary in the interpretation of high %RF values. In patients with atypical symptoms of CTS and normal conventional studies, pathologically increased %RF values pose a problem of interpretation. This method for identifying a peripheral nerve lesion does not allow precise localization of its site, and similar changes would be found with a more proximal median nerve lesion. The contribution of any associated proximal neural lesion to the abnormal %RF value has not been evaluated. It is clear that different skeletal muscles have their own individual %RF and NFR values in the healthy state, and this must be taken account of before the effect of a peripheral nerve lesion can be assessed.[31]

To minimize time and expense in reaching an electrodiagnosis of CTS, it is recommended that the DML be first measured. If this does not provide an abnormal value (approximately 66% of cases), and the terminal latency index is within normal limits, the SAWPL (or equivalent transtunnel assessment) should be measured. If this value proves to be within normal limits, F latencies across the carpal tunnel should be measured, and if these values are not clearly abnormal, the %RF value for the nerve should be calculated.

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References

1. Kugelberg E. "Injury activity" and "trigger zones" in human nerves. Brain 1946;69:310-322.
2. Buchtal F, Rosenfalck A, Trojaborg W. Electrophysiological findings in entrapment of the median nerve at wrist and elbow. J Neurol Neurosurg Psychiatry 1974;37:340-360.
3. Eklund G. A new electrodiagnostic procedure for measuring sensory nerve conduction across the carpal tunnel. Ups J Med Sci 1975;80:63-64.
4. Daube JR. Percutaneous palmar median nerve stimulation for carpal tunnel syndrome. Abstract. Electroencephalogr Clin Neurophysiol 1977;43:139-140.
5. Kimura J. A method for determining median nerve conduction velocity across the carpal tunnel. J Neurol Sci 1978;35:1-10.
6. Kimura J. The carpal tunnel syndrome: localization of conduction abnormalities within the distal segment of the median nerve. Brain 1979;102:619-635.
7. Roth G. Vitesse de conduction motrice du nerf median dans le canal carpien. Annales de Medecine Physique 1970;13:117-132.
8. Wiederholt WC. Median nerve conduction velocity in sensory fibers through carpal tunnel. Arch Phys Med Rehabil 1970;51:328-330.
9. Buchtal F, Rosenfalck A. Sensory conduction from digit to palm and from palm to wrist in the carpal tunnel syndrome. J Neurol Neurosurg Psychiatry 1971;34:243-252.
10. Mills KR. Orthodromic sensory action potentials from palmar stimulation in the diagnosis of carpal tunnel syndrome. J Neurol Neurosurg Psychiatry 1985;48:250-255.
11. Egloff-Baer AS, Shahani BT, Young RR. Usefulness of late response studies in diagnosis of entrapment neuropathies. Electroencephalogr Clin Neurophysiol 1978;45:16P.
12. Eisen A, Schomer D, Melmed C. The application of F-wave measurements in the differentiation of proximal and distal upper limb entrapments. Neurology 1977;27:662-668.
13. Maccabee PJ, Shahani BT, Young RR. Usefulness of double simultaneous recording (DSR) and F response studies in the diagnosis of carpal tunnel syndrome (C.T.S.). Electroencephalogr Clin Neurophysiol 1980;49:18P.
14. Loong SC, Seah CS. Comparison of median and ulnar sensory nerve action potentials in the diagnosis of the carpal tunnel syndrome. J Neurol Neurosurg Psychiatry 1971;34:750-754.
15. Renshaw B. Influence of discharge of motoneurones upon excitation of neighbouring motoneurones. J Neurophysiol 1941;4:167-180.
16. Magladery JW, McDougal DB. Electrophysiological studies of nerve and reflex activity in normal man. I. Identification of certain reflexes in the electromyogram and the conduction velocity of peripheral nerve fibers. Bull Johns Hopkins Hospital 1950;86:265-290.
17. Schiller HH, Stålberg E. Responses studied with single fibre EMG in normal subjects and spastic patients. J Neurol Neurosurg Psychiatry 1978;41:45-53.
18. Knezevic W, Mastaglia FL, Thickbroom GW, Carroll WM. Changes in alpha-motoneurone excitability during and after voluntary muscle contraction. Electroencephalogr Clin Neurophysiol 1985;61:S63. Abstracts of the XIth International Congress of Electroencephalography and Clinical Neurophysiology. London: Elsevier, 1985.
19. Thomas PK. Motor nerve conduction in the carpal tunnel syndrome. Neurology 1960;10:1045-1050.
20. Phalen GS. Spontaneous compression of the median nerve at the wrist. JAMA 1951;145:1128-1133.
21. Diagnosis of the carpal tunnel syndrome. Editorial. Lancet 1985;1:854-855.
22. Simpson JA. Electrical signs in the diagnosis of carpal tunnel and related syndromes. J Neurol Neurosurg Psychiatry 1956;19:275-280.
23. Phalen GS. Reflections on 21 years' experience with the carpal tunnel syndrome. JAMA 1970;212:1365-1367.
24. Phalen GS. The carpal tunnel syndrome: seventeen years' experience in diagnosis and treatment of six hundred and fifty-four hands. J Bone Joint Surg (Am) 1966;48A:211-228.
25. Aebi-Ochsner CL, Ludin HP. Das Karpaltunnelsyndrom: klinische Symtomatologie und elektrophysiologische Befunde. Neurol Psychiatr (Bucur) 1979;47:307-319.
26. Entin MA. Carpal tunnel syndrome and its variants. Surg Clin N Am 1968;48:1097-1111.
27. Gilliat RW, Sears TA. Sensory nerve action potentials in patients with peripheral nerve lesions. J Neurol Neurosurg Psychiatry 1958;21:109-118.
28. Muhlau G, Both R, Kunath H. Carpal tunnel syndrome: course and prognosis. J Neurol 1984;231:83-86.
29. Fullerton PM, Gilliat RW. Axon reflexes in human motor nerve fibres. J Neurol Neurosurg Psychiatry 1965;28:1-11.
30. Dawson GD, Scott JW. The recording of nerve action potentials through the skin in man. J Neurol Neurosurg Psychiatry 1949;12:259-267.
31. Macleod WN. Variations in neuronal response to antidromic invasion (F-response) of spinal α motor neurone pools subserving abductor pollicis brevis, abductor digiti minimi, and extensor digitorum brevis in man. Journal of Physiology 1986;59P:380.

PP572

MRI and Electrophysiologic Evidence Suggesting a Secondary Functional Disturbance of the Central Nervous System in Fisher's Syndrome

William MacLeod, Dundee, Scotland, UK; and Graham R. Cherryman, Aberdeen, Scotland

Controversy continues over the pathophysiology of the clinical syndrome of ataxia, areflexia, and ophthalmoplegia. Fisher "reluctantly interpreted the clinical signs as an unusual disturbance of peripheral neurons". The concept of a disordered peripheral system generating "counterfeit" central signs remains important. Other reports have described abnormalities in conventional nerve conduction studies (NCS), and mismatched muscle spindle and joint capsule sensory input may be the peripheral basis of the "cerebellar" ataxia. Here, electrophysiologic evidence of a modification of the "central motor excitatory state" is provided in two cases. The back-firing characteristics of the motor neuron pools of abductor pollicis brevis and abductor digiti minimi were quantified and, when expressed as a % Repeater F-wave value, were significantly deranged (compared with data from over 100 healthy control subjects). MRI and CT of brainstem were normal. Clinical and conventional NCS data are presented. A functional disturbance of the central nervous system resulting from peripheral nerve dysfunction is discussed as is the application of F-wave analysis in differentiating a tectal plate lesion from Fisher's syndrome.

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NEUROPHYSIOLOGY

MACLEOD, W.N. (Massachusetts General Hospital, Boston, MA); SHAHANI, B.: **New Electrodiagnostic Abnormalities in Syringomyelia.**

In syringomyelia the electrodiagnostic abnormalities described include EMG signs of denervation/reinnervation, delayed F responses, small compound muscle action potentials, the release of the H reflex, delayed or absent somatosensory evoked potentials and delay or absence of the R2 component of the blink reflex. We describe 2 additional findings: 1) an alteration in the backfiring frequencies of ipsisegmental anterior horn cells (AHC) in response to antidromic nerve volleys and 2) High frequency repetitive discharges in ipsisegmental myotomes. The F generators of abductor digiti minimi (ADM) were characterized in 3 cases of cervico-dorsal syringomyelia and in over 100 control subjects by applying 100 stimuli at 1 Hz. to each ulnar nerve under test and calculating the frequency of same latency, same wave form F responses as a % of the total number of F responses obtained. A reduction in the number of active F generators and an increased frequency of backfiring in a small number of AHC's were found in syringomyelia. This may result from a reduction in the number of AHC's in the ADM pool and/or modification of AHC membrane characteristics via altered spinal input or damaged intraspinal connections.

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Carpal tunnel syndrome (CTS) mimicking cervical spondylosis (CS): a clinical and electrophysiological study. W. N. Macleod. Dundee. Scotland. UK

Signs and symptoms of CS and CTS overlap. Without definitive clinical signs misdiagnosis could result. I studied 9 symptomatic arms in 7 patients. < 55 years old. with a diagnosis of CS made previously (1985) by an orthopaedic specialist. All had pain/altered sensation in arm/hand without neurological signs. I have assessed the prevalence of (1) median nerve (MN) dysfunction. (2) a "double crush". (3) C5/6 radiculopathy. (4) plexopathy (1–4: electrodiagnostic tests) and assessed clinical signs/symptoms > 2 years after diagnosis of CS.

Methods. Tests: EMG C5.6.7.8 paraspinal. abductor policis brevis (APB) first dorsal interosseous muscles (ADM). F wave latencies and proximal segment F wave conduction velocity (CV) to APB. ADM/ sensory potentials: radial. ulnar (U) medial and lateral antebrachial cutaneous/antidromic wrist-palm latency. distal motor latency. % repeater F wave MN/mixed nerve CV palm-wrist. U. MN.

Results. 66% (6/9) of MNs had an electrodiagnostic abnormality and no evidence of. motor radiculopathy/double crush lesion/plexopathy. One had APB denervation. Since initial CS diagnosis 2 have developed numb waking. 1 a flick sign and 1 hypalgesia distal to the index proximal interphalangeal joint.

Conclusion. Nonspecific brachalgia and dysaethesiae (C6 ± C5. C7. C8) can be difficult to diagnose. CTS may mimic symptoms more typical of CS.